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(54) Title: **NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION, ASSESSMENT, PREVENTION, AND THERAPY OF OVARIAN CANCER**

(57) Abstract: The invention relates to newly discovered nucleic acid molecules and proteins associated with ovarian cancer. Compositions, kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.

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NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION,  
ASSESSMENT, PREVENTION, AND THERAPY OF  
OVARIAN CANCER

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## RELATED APPLICATIONS

The present application claims priority from U.S. provisional patent application serial no. 60/276,025, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/325,149, filed on September 26, 2001. The present application also claims priority from U.S. provisional  
10 patent application serial no. 60/276,026, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/324,967, filed September 26, 2001. The present application additionally claims priority from U.S. provisional patent application serial no. 60/311,732, filed August 10, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent  
15 application serial no. 60/325,102, filed September 26, 2001. The present application also claims priority from U.S. provisional patent application serial no. 60/323,580, filed September 19, 2001. All of the above applications are expressly incorporated by reference.

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## FIELD OF THE INVENTION

The field of the invention is ovarian cancer, including diagnosis, characterization, management, and therapy of ovarian cancer.

## BACKGROUND OF THE INVENTION

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Ovarian cancer is responsible for significant morbidity and mortality in populations around the world. Ovarian cancer is classified, on the basis of clinical and pathological features, in three groups, namely epithelial ovarian cancer (EOC; >90% of ovarian cancer in Western countries), germ cell tumors (*circa* 2-3% of ovarian cancer), and stromal ovarian cancer (*circa* 5% of ovarian cancer; Ozols *et al.*, 1997, *Cancer Principles and Practice of Oncology*, 5th ed., DeVita *et al.*, Eds. pp. 1502). Relative to  
30 EOC, germ cell tumors and stromal ovarian cancers are more easily detected and treated



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at an early stage, translating into higher/better survival rates for patients afflicted with these two types of ovarian cancer.

There are numerous types of ovarian tumors, some of which are benign, and others of which are malignant. Treatment (including non-treatment) options and predictions of patient outcome depend on accurate classification of the ovarian cancer. Ovarian cancers are named according to the type of cells from which the cancer is derived and whether the ovarian cancer is benign or malignant. Recognized histological tumor types include, for example, serous, mucinous, endometrioid, and clear cell tumors. In addition, ovarian cancers are classified according to recognized grade and stage scales.

In grade I, the tumor tissue is well differentiated. In grade II, tumor tissue is moderately well differentiated. In grade III, the tumor tissue is poorly differentiated. This grade correlates with a less favorable prognosis than grades I and II. Stage I is generally confined within the capsule surrounding one (stage IA) or both (stage IB) ovaries, although in some stage I (*i.e.* stage IC) cancers, malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. Stage II involves extension or metastasis of the tumor from one or both ovaries to other pelvic structures. In stage IIA, the tumor extends or has metastasized to the uterus, the fallopian tubes, or both. Stage IIB involves extension of the tumor to the pelvis. Stage IIC is stage IIA or IIB in which malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. In stage III, the tumor comprises at least one malignant extension to the small bowel or the omentum, has formed extrapelvic peritoneal implants of microscopic (stage IIIA) or macroscopic (< 2 centimeter diameter, stage IIIB; > 2 centimeter diameter, stage IIIC) size, or has metastasized to a retroperitoneal or inguinal lymph node (an alternate indicator of stage IIIC). In stage IV, distant (*i.e.* non-peritoneal) metastases of the tumor can be detected.

The durations of the various stages of ovarian cancer are not presently known, but are believed to be at least about a year each (Richart *et al.*, 1969, *Am. J. Obstet. Gynecol.* 105:386). Prognosis declines with increasing stage designation. For example, 5-year survival rates for patients diagnosed with stage I, II, III, and IV ovarian cancer are 80%, 57%, 25%, and 8%, respectively.

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Despite being the third most prevalent gynecological cancer, ovarian cancer is the leading cause of death among those afflicted with gynecological cancers. The disproportionate mortality of ovarian cancer is attributable to a substantial absence of symptoms among those afflicted with early-stage ovarian cancer and to difficulty  
5 diagnosing ovarian cancer at an early stage. Patients afflicted with ovarian cancer most often present with non-specific complaints, such as abnormal vaginal bleeding, gastrointestinal symptoms, urinary tract symptoms, lower abdominal pain, and generalized abdominal distension. These patients rarely present with paraneoplastic symptoms or with symptoms which clearly indicate their affliction. Presently, less than  
10 about 40% of patients afflicted with ovarian cancer present with stage I or stage II. Management of ovarian cancer would be significantly enhanced if the disease could be detected at an earlier stage, when treatments are much more generally efficacious.

Ovarian cancer may be diagnosed, in part, by collecting a routine medical history from a patient and by performing physical examination, x-ray examination, and  
15 chemical and hematological studies on the patient. Hematological tests which may be indicative of ovarian cancer in a patient include analyses of serum levels of proteins designated CA125 and DF3 and plasma levels of lysophosphatidic acid (LPA). Palpation of the ovaries and ultrasound techniques (particularly including endovaginal ultrasound and color Doppler flow ultrasound techniques) can aid detection of ovarian  
20 tumors and differentiation of ovarian cancer from benign ovarian cysts. However, a definitive diagnosis of ovarian cancer typically requires performing exploratory laparotomy of the patient.

Potential tests for the detection of ovarian cancer (*e.g.*, screening, reflex or monitoring) may be characterized by a number of factors. The "sensitivity" of an  
25 assay refers to the probability that the test will yield a positive result in an individual afflicted with ovarian cancer. The "specificity" of an assay refers to the probability that the test will yield a negative result in an individual not afflicted with ovarian cancer. The "positive predictive value" (PPV) of an assay is the ratio of true positive results (*i.e.* positive assay results for patients afflicted with ovarian cancer) to all positive results  
30 (*i.e.* positive assay results for patients afflicted with ovarian cancer + positive assay results for patients not afflicted with ovarian cancer). It has been estimated that in order for an assay to be an appropriate population-wide screening tool for ovarian cancer the

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assay must have a PPV of at least about 10% (Rosenthal *et al.*, 1998, *Sem. Oncol.* 25:315-325). It would thus be desirable for a screening assay for detecting ovarian cancer in patients to have a high sensitivity and a high PPV. Monitoring and reflex tests would also require appropriate specifications.

5           Owing to the cost, limited sensitivity, and limited specificity of known methods of detecting ovarian cancer, screening is not presently performed for the general population. In addition, the need to perform laparotomy in order to diagnose ovarian cancer in patients who screen positive for indications of ovarian cancer limits the desirability of population-wide screening, such that a PPV even greater than 10%  
10    would be desirable.

          Prior use of serum CA125 level as a diagnostic marker for ovarian cancer indicated that this method exhibited insufficient specificity for use as a general screening method. Use of a refined algorithm for interpreting CA125 levels in serial retrospective samples obtained from patients improved the specificity of the method  
15    without shifting detection of ovarian cancer to an earlier stage (Skakes, 1995, *Cancer* 76:2004). Screening for LPA to detect gynecological cancers including ovarian cancer exhibited a sensitivity of about 96% and a specificity of about 89%. However, CA125-based screening methods and LPA-based screening methods are hampered by the presence of CA125 and LPA, respectively, in the serum of patients afflicted with  
20    conditions other than ovarian cancer. For example, serum CA125 levels are known to be associated with menstruation, pregnancy, gastrointestinal and hepatic conditions such as colitis and cirrhosis, pericarditis, renal disease, and various non-ovarian malignancies. Serum LPA is known, for example, to be affected by the presence of non-ovarian gynecological malignancies. A screening method having a greater specificity for  
25    ovarian cancer than the current screening methods for CA125 and LPA could provide a population-wide screening for early stage ovarian cancer.

          Presently greater than about 60% of ovarian cancers diagnosed in patients are stage III or stage IV cancers. Treatment at these stages is largely limited to cytoreductive surgery (when feasible) and chemotherapy, both of which aim to slow the  
30    spread and development of metastasized tumor. Substantially all late stage ovarian cancer patients currently undergo combination chemotherapy as primary treatment, usually a combination of a platinum compound and a taxane. Median survival for

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responding patients is about one year. Combination chemotherapy involving agents such as doxorubicin, cyclophosphamide, cisplatin, hexamethylmelamine, paclitaxel, and methotrexate may improve survival rates in these groups, relative to single-agent therapies. Various recently-developed chemotherapeutic agents and treatment regimens have also demonstrated usefulness for treatment of advanced ovarian cancer. For example, use of the topoisomerase I inhibitor topectan, use of amifostine to minimize chemotherapeutic side effects, and use of intraperitoneal chemotherapy for patients having peritoneally implanted tumors have demonstrated at least limited utility. Presently, however, the 5-year survival rate for patients afflicted with stage III ovarian cancer is 25%, and the survival rate for patients afflicted with stage IV ovarian cancer is 8%.

In summary, the earlier ovarian cancer is detected, the aggressiveness of therapeutic intervention and the side effects associated with therapeutic intervention are minimized. More importantly, the earlier the cancer is detected, the survival rate and quality of life of ovarian cancer patients is enhanced. Thus, a pressing need exists for methods of detecting ovarian cancer as early as possible. There also exists a need for methods of detecting recurrence of ovarian cancer as well as methods for predicting and monitoring the efficacy of treatment. There further exists a need for new therapeutic methods for treating ovarian cancer. The present invention satisfies these needs.

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#### SUMMARY OF THE INVENTION

The invention relates to cancer markers (hereinafter "markers" or "markers of the inventions"), which are listed in Tables 1-3. The invention provides nucleic acids and proteins that are encoded by or correspond to the markers (hereinafter "marker nucleic acids" and "marker proteins," respectively). The invention further provides antibodies, antibody derivatives and antibody fragments which bind specifically with such proteins and/or fragments of the proteins.

In one aspect, the invention relates to various diagnostic, monitoring, test and other methods related to ovarian cancer detection and therapy. In one embodiment, the invention provides a diagnostic method of assessing whether a patient has ovarian cancer or has higher than normal risk for developing ovarian cancer, comprising the steps of comparing the level of expression of a marker of the invention in a patient

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sample and the normal level of expression of the marker in a control, *e.g.*, a sample from a patient without ovarian cancer. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer or has higher than normal risk for developing ovarian cancer.

In a preferred embodiment of the diagnostic method, the marker is over-expressed by at least two-fold in at least about 20% of stage I ovarian cancer patients, stage II ovarian cancer patients, stage III ovarian cancer patients, stage IV ovarian cancer patients, grade I ovarian cancer patients, grade II ovarian cancer patients, grade III ovarian cancer patients, epithelial ovarian cancer patients, stromal ovarian cancer patients, germ cell ovarian cancer patients, malignant ovarian cancer patients, benign ovarian cancer patients, serous neoplasm ovarian cancer patients, mucinous neoplasm ovarian cancer patients, endometrioid neoplasm ovarian cancer patients and/or clear cell neoplasm ovarian cancer patients.

The diagnostic methods of the present invention are particularly useful for patients with an identified pelvic mass or symptoms associated with ovarian cancer. The methods of the present invention can also be of particular use with patients having an enhanced risk of developing ovarian cancer (*e.g.*, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene, and patients at least about 50 years of age).

In a preferred diagnostic method of assessing whether a patient is afflicted with ovarian cancer (*e.g.*, new detection ("screening"), detection of recurrence, reflex testing), the method comprises comparing:

- a) the level of expression of a marker of the invention in a patient sample,
- and
- b) the normal level of expression of the marker in a control non-ovarian cancer sample.

A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

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The invention also provides diagnostic methods for assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient. Such methods comprise comparing:

- 5 a) expression of a marker of the invention in a first sample obtained from the patient prior to providing at least a portion of the therapy to the patient, and
- b) expression of the marker in a second sample obtained from the patient following provision of the portion of the therapy.

10 A significantly lower level of expression of the marker in the second sample relative to that in the first sample is an indication that the therapy is efficacious for inhibiting ovarian cancer in the patient.

It will be appreciated that in these methods the "therapy" may be any therapy for treating ovarian cancer including, but not limited to, chemotherapy, radiation therapy, surgical removal of tumor tissue, gene therapy and biologic therapy such as the  
15 administering of antibodies and chemokines. Thus, the methods of the invention may be used to evaluate a patient before, during and after therapy, for example, to evaluate the reduction in tumor burden.

In a preferred embodiment, the diagnostic methods of the present invention are directed to therapy using a chemical or biologic agent. These methods  
20 comprise comparing:

- a) expression of a marker of the invention in a first sample obtained from the patient and maintained in the presence of the chemical or biologic agent, and
- 25 b) expression of the marker in a second sample obtained from the patient and maintained in the absence of the agent.

A significantly lower level of expression of the marker in the first sample relative to that in the second sample is an indication that the agent is efficacious for inhibiting ovarian cancer in the patient. In one embodiment, the first and second samples can be portions of a single sample obtained from the patient or portions of pooled samples obtained  
30 from the patient.

The invention additionally provides a monitoring method for assessing the progression of ovarian cancer in a patient, the method comprising:

- a) detecting in a patient sample at a first time point, the expression of a marker of the invention;
- 5       b) repeating step a) at a subsequent time point in time; and
- c) comparing the level of expression detected in steps a) and b), and therefrom monitoring the progression of ovarian cancer in the patient.

A significantly higher level of expression of the marker in the sample at the subsequent time point from that of the sample at the first time point is an indication that the ovarian cancer has progressed, whereas a significantly lower level of expression is an indication  
10       that the ovarian cancer has regressed.

The invention further provides a diagnostic method for determining whether ovarian cancer has metastasized or is likely to metastasize in the future, the method comprising comparing:

- 15       a) the level of expression of a marker of the invention in a patient sample, and
- b) the normal level (or non-metastatic level) of expression of the marker in a control sample.

A significantly higher level of expression in the patient sample as compared to the  
20       normal level (or non-metastatic level) is an indication that the ovarian cancer has metastasized or is likely to metastasize in the future.

The invention moreover provides a test method for selecting a composition for inhibiting ovarian cancer in a patient. This method comprises the steps of:

- 25       a) obtaining a sample comprising cancer cells from the patient;
- b) separately maintaining aliquots of the sample in the presence of a plurality of test compositions;
- c) comparing expression of a marker of the invention in each of the aliquots; and
- 30       d) selecting one of the test compositions which significantly reduces the level of expression of the marker in the aliquot containing that test

composition, relative to the levels of expression of the marker in the presence of the other test compositions.

The invention additionally provides a test method of assessing the ovarian carcinogenic potential of a compound. This method comprises the steps of:

- 5           a) maintaining separate aliquots of ovarian cells in the presence and absence of the compound; and
- b) comparing expression of a marker of the invention in each of the aliquots.

10           A significantly higher level of expression of the marker in the aliquot maintained in the presence of the compound, relative to that of the aliquot maintained in the absence of the compound, is an indication that the compound possesses ovarian carcinogenic potential.

In addition, the invention further provides a method of inhibiting ovarian cancer in a patient. This method comprises the steps of:

- 15           a) obtaining a sample comprising cancer cells from the patient;
- b) separately maintaining aliquots of the sample in the presence of a plurality of compositions;
- c) comparing expression of a marker of the invention in each of the aliquots; and
- 20           d) administering to the patient at least one of the compositions which significantly lowers the level of expression of the marker in the aliquot containing that composition, relative to the levels of expression of the marker in the presence of the other compositions.

In the aforementioned methods, the samples or patient samples comprise cells obtained from the patient. The cells may be found in an ovarian tissue sample

25   collected, for example, by an ovarian tissue biopsy or histology section. In one embodiment, the patient sample is an ovary-associated body fluid. Such fluids include, for example, blood fluids, lymph, ascites fluids, gynecological fluids, cystic fluids, urine, and fluids collected by peritoneal rinsing. In another embodiment, the sample comprises cells obtained from the patient. In this embodiment, the cells may be found in

30   a fluid selected from the group consisting of a fluid collected by peritoneal rinsing, a fluid collected by uterine rinsing, a uterine fluid, a uterine exudate, a pleural fluid, and an ovarian exudate. In a further embodiment, the patient sample is *in vivo*.



According to the invention, the level of expression of a marker of the invention in a sample can be assessed, for example, by detecting the presence in the sample of:

- 5       • the corresponding marker protein or a fragment of the protein (*e.g.* by using a reagent, such as an antibody, an antibody derivative, an antibody fragment or single-chain antibody, which binds specifically with the protein or protein fragment).
- 10       • the corresponding marker nucleic acid or a fragment of the nucleic acid (*e.g.* by contacting transcribed polynucleotides obtained from the sample with a substrate having affixed thereto one or more nucleic acids having the entire or a segment of the sequence or a complement thereof)
- a metabolite which is produced directly (*i.e.*, catalyzed) or indirectly by the corresponding marker protein.

According to the invention, any of the aforementioned methods may be performed using a plurality (*e.g.* 2, 3, 5, or 10 or more) of ovarian cancer markers, including ovarian cancer markers known in the art. In such methods, the level of expression in the sample of each of a plurality of markers, at least one of which is a marker of the invention, is compared with the normal level of expression of each of the plurality of markers in samples of the same type obtained from control humans not afflicted with ovarian cancer. A significantly altered (*i.e.*, increased or decreased as specified in the above-described methods using a single marker) level of expression in the sample of one or more markers of the invention, or some combination thereof, relative to that marker's corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. For all of the aforementioned methods, the marker(s) are preferably selected such that the positive predictive value of the method is at least about 10%.

In a further aspect, the invention provides an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein or a fragment of the protein. The invention also provides methods for making such antibody, antibody derivative, and antibody fragment. Such methods may comprise immunizing a mammal with a protein or peptide comprising the entirety, or a segment of 10 amino acids or more, of a marker protein, wherein the protein or peptide may be obtained from

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a cell or by chemical synthesis. The methods of the invention also encompass producing monoclonal and single-chain antibodies, which would further comprise isolating splenocytes from the immunized mammal, fusing the isolated splenocytes with an immortalized cell line to form hybridomas, and screening individual hybridomas for those that produce an antibody that binds specifically with a marker protein or a fragment of the protein.

In another aspect, the invention relates to various diagnostic and test kits. In one embodiment, the invention provides a kit for assessing whether a patient is afflicted with ovarian cancer. The kit comprises a reagent for assessing expression of a marker of the invention. In another embodiment, the invention provides a kit for assessing the suitability of a chemical or biologic agent for inhibiting an ovarian cancer in a patient. Such kit comprises a reagent for assessing expression of a marker of the invention, and may also comprise one or more of such agents. In a further embodiment, the invention provides kits for assessing the presence of ovarian cancer cells or treating ovarian cancers. Such kits comprise an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein, or a fragment of the protein. Such kits may also comprise a plurality of antibodies, antibody derivatives, or antibody fragments wherein the plurality of such antibody agents binds specifically with a marker protein, or a fragment of the protein.

In an additional embodiment, the invention also provides a kit for assessing the presence of ovarian cancer cells, wherein the kit comprises a nucleic acid probe that binds specifically with a marker nucleic acid or a fragment of the nucleic acid. The kit may also comprise a plurality of probes, wherein each of the probes binds specifically with a marker nucleic acid, or a fragment of the nucleic acid.

In a further aspect, the invention relates to methods for treating a patient afflicted with ovarian cancer or at risk of developing ovarian cancer. Such methods may comprise reducing the expression and/or interfering with the biological function of a marker of the invention. In one embodiment, the method comprises providing to the patient an antisense oligonucleotide or polynucleotide complementary to a marker nucleic acid, or a segment thereof. For example, an antisense polynucleotide may be provided to the patient through the delivery of a vector that expresses an antisense polynucleotide of a marker nucleic acid or a fragment thereof. In another embodiment,

the method comprises providing to the patient an antibody, an antibody derivative, or antibody fragment, which binds specifically with a marker protein or a fragment of the protein. In a preferred embodiment, the antibody, antibody derivative or antibody fragment binds specifically with a protein having the sequence of any of the markers  
5 listed in Table 1, or a fragment of such a protein.

It will be appreciated that the methods and kits of the present invention may also include known cancer markers including known ovarian cancer markers. It will further be appreciated that the methods and kits may be used to identify cancers other than ovarian cancer.

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### BRIEF DESCRIPTION OF THE DRAWINGS

*Figure 1* depicts a graph which represents the results of the TaqMan® expression study.

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### DETAILED DESCRIPTION OF THE INVENTION

The invention relates to newly discovered markers, identified in Tables 1-3, that are associated with the cancerous state of ovarian cells. It has been discovered that the higher than normal level of expression of any of these markers or combination of these markers correlates with the presence of ovarian cancer in a patient. Methods  
20 are provided for detecting the presence of ovarian cancer in a sample, the absence of ovarian cancer in a sample, the stage of an ovarian cancer, and with other characteristics of ovarian cancer that are relevant to prevention, diagnosis, characterization, and therapy of ovarian cancer in a patient. Methods of treating ovarian cancer are also provided.

Tables 1-3 list the markers of the present invention. In the Tables the  
25 markers are identified with a name ("Marker"), the name the gene is commonly known by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein  
30 coding sequence within the cDNA sequence ("CDS").

Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide

and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

In addition to their use in ovarian cancer, it has been found that the markers of the present invention may be used in the diagnosis, characterization, management, and therapy of additional diseases. For example, OV65 (SEQ ID NOS: 305 and 306), M593 (SEQ ID NOS: 307 and 308) and M594 (SEQ ID NOS: 309 and 310), are spondin molecules, and have one or more of the following activities: (1) neural cell adhesion and (2) neurite extension and can thus be used in, for example, the diagnosis and treatment of brain and CNS related disorders. Such brain and CNS related disorders include, but are not limited to, bacterial and viral meningitis, Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis. In another example, OV65, M593 and M594 polypeptides, nucleic acids, and modulators thereof can be used to treat disorders of the brain, such as cerebral edema, hydrocephalus, brain herniations, iatrogenic disease (due to, *e.g.*, infection, toxins, or drugs), inflammations (*e.g.*, bacterial and viral meningitis, encephalitis, and cerebral toxoplasmosis), cerebrovascular diseases (*e.g.*, hypoxia, ischemia, infarction, intracranial hemorrhage, vascular malformations, and hypertensive encephalopathy), and tumors (*e.g.*, neuroglial tumors, neuronal tumors, tumors of pineal cells, meningeal tumors, primary and secondary lymphomas, intracranial tumors, and medulloblastoma), and to treat injury or trauma to the brain.

OV25 (SEQ ID NOS: 360 and 361), an HE4 protein, has one or more of the following activities: (1) sperm maturation and (2) inhibition of extracellular proteases and can thus be used in, for example, the treatment and diagnosis of diseases and disorders relating to spermatogenesis. For example, OV25 polypeptides, nucleic acids, and modulators thereof can be used to treat testicular disorders, such as unilateral testicular enlargement (*e.g.*, nontuberculous, granulomatous orchitis); inflammatory diseases resulting in testicular dysfunction (*e.g.*, gonorrhea and mumps); cryptorchidism; sperm cell disorders (*e.g.*, immotile cilia syndrome and germinal cell aplasia); acquired testicular defects (*e.g.*, viral orchitis); and tumors (*e.g.*, germ cell tumors, interstitial cell tumors, androblastoma, testicular lymphoma and adenomatoid tumors).

OV52 (SEQ ID NOS: 190 and 191), a Pump-1 proteinase, has been found to have one or more of the following activities: (1) breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and remodeling, as well as in (2) disease processes, such as arthritis, and metastasis. Hence, 5 OV52 nucleic acids, proteins, and modulators thereof can be used to modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thromboasthenia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of 10 neutrophils to sites of extravascular inflammation), connective tissue disorders, arthritis, disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

M604 (SEQ ID NOS: 48 and 49), OV10 (SEQ ID NOS: 50 and 51), and M360 (SEQ ID NOS: 52 and 53), are Claudin molecules which have one or more of the 15 following activities: (1) it elicits fluid accumulation in the intestinal tract by altering the membrane permeability of intestinal epithelial cells and (2) thus acts as the causative agent of diarrhea. The polypeptides, nucleic acids, and modulators thereof can be used to treat colonic disorders, such as congenital anomalies (*e.g.*, megacolon and imperforate anus), idiopathic disorders (*e.g.*, diverticular disease and melanosis coli), vascular 20 lesions (*e.g.*, ischemic colitis, hemorrhoids, angiodysplasia), inflammatory diseases (*e.g.*, colitis (*e.g.*, idiopathic ulcerative colitis, pseudomembranous colitis), and lymphopathia venereum), Crohn's disease, and tumors (*e.g.*, hyperplastic polyps, adenomatous polyps, bronchogenic cancer, colonic carcinoma, squamous cell carcinoma, adenoacanthomas, sarcomas, lymphomas, argentaffinomas, carcinoids, and 25 melanocarcinomas).

OV48 (SEQ ID NOS: 226 and 227), OV49 (SEQ ID NOS: 228 and 229) and OV50 (SEQ ID NOS: 230 and 231), markers for an osteopontin protein, have one or more of the following activities: (1) they act as a vessel extracellular matrix protein involved in calcification and (2) atherosclerosis. Hence, OV48, OV49 and OV50 30 nucleic acids, proteins, and modulators thereof can be used to treat heart disorders, *e.g.*, ischemic heart disease, atherosclerosis, hypertension, angina pectoris, Hypertrophic Cardiomyopathy, and congenital heart disease. They can also be used to treat

cardiovascular disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital  
5 heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cardiomyopathy).

OV37 (SEQ ID NOS: 176 and 177), a lipocalin marker, is known to be a component of the neutrophil gelatinase complex. OV37 nucleic acids, proteins, and  
10 modulators thereof can be used to modulate the proliferation, differentiation, and/or function of leukocytes. Thus, OV37 nucleic acids, proteins, and modulators thereof can be used to treat bone marrow, blood, and hematopoietic associated diseases and disorders, *e.g.*, acute myeloid leukemia, hemophilia, leukemia, anemia (*e.g.*, sickle cell anemia), and thalassemia. OV37 polypeptides, nucleic acids, and modulators thereof can  
15 be used to treat leukocytic disorders, such as leukopenias (*e.g.*, neutropenia, monocytopenia, lymphopenia, and granulocytopenia), leukocytosis (*e.g.*, granulocytosis, lymphocytosis, eosinophilia, monocytosis, acute and chronic lymphadenitis), malignant lymphomas (*e.g.*, Non-Hodgkin's lymphomas, Hodgkin's lymphomas, leukemias, agnogenic myeloid metaplasia, multiple myeloma, plasmacytoma, Waldenstrom's  
20 macroglobulinemia, heavy-chain disease, monoclonal gammopathy, histiocytoses, eosinophilic granuloma, and angioimmunoblastic lymphadenopathy).

OV2 (SEQ ID NOS: 285 and 286), is known to be a protease inhibitor, which is associated with emphysema and liver disease. Hence OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat pulmonary  
25 (lung) disorders, such as atelectasis, cystic fibrosis, rheumatoid lung disease, pulmonary congestion or edema, chronic obstructive airway disease (*e.g.*, emphysema, chronic bronchitis, bronchial asthma, and bronchiectasis), diffuse interstitial diseases (*e.g.*, sarcoidosis, pneumoconiosis, hypersensitivity pneumonitis, bronchiolitis, Goodpasture's syndrome, idiopathic pulmonary fibrosis, idiopathic pulmonary hemosiderosis,  
30 pulmonary alveolar proteinosis, desquamative interstitial pneumonitis, chronic interstitial pneumonia, fibrosing alveolitis, hamman-rich syndrome, pulmonary eosinophilia, diffuse interstitial fibrosis, Wegener's granulomatosis, lymphomatoid

granulomatosis, and lipid pneumonia), or tumors (*e.g.*, bronchogenic carcinoma, bronchioloalveolar carcinoma, bronchial carcinoid, hamartoma, and mesenchymal tumors). In another example, OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat hepatic (liver) disorders, such as jaundice, hepatic failure, hereditary hyperbilirubinemias (*e.g.*, Gilbert's syndrome, Crigler-Najjar syndromes and Dubin-Johnson and Rotor's syndromes), hepatic circulatory disorders (*e.g.*, hepatic vein thrombosis and portal vein obstruction and thrombosis), hepatitis (*e.g.*, chronic active hepatitis, acute viral hepatitis, and toxic and drug-induced hepatitis), cirrhosis (*e.g.*, alcoholic cirrhosis, biliary cirrhosis, and hemochromatosis), or malignant tumors (*e.g.*, primary carcinoma, hepatoma, hepatoblastoma, liver cysts, and angiosarcoma).

OV32 (SEQ ID NOS: 166 and 167) and OV33 (SEQ ID NOS: 168 and 169), kallikrein markers, are useful in detection of primary mammary carcinomas, as well as primary ovarian cancers. Hence, OV32 and OV33 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat ovarian disorders, such as ovarian endometriosis, non-neoplastic cysts (*e.g.*, follicular and luteal cysts and polycystic ovaries) and tumors (*e.g.*, carcinomas, tumors of surface epithelium, germ cell tumors, ovarian fibroma, sex cord-stromal tumors, and ovarian cancers (*e.g.*, metastatic carcinomas, and ovarian teratoma)).

OV68 (SEQ ID NOS: 192 and 193), OV69 (SEQ ID NOS: 194 and 195), OV70 (SEQ ID NOS: 196 and 197), OV71 (SEQ ID NOS: 198 and 199), OV72 (SEQ ID NOS: 200 and 201), OV41 (SEQ ID NOS: 202 and 203), OV42 (SEQ ID NOS: 204 and 205), OV43 (SEQ ID NOS: 206 and 205), OV44 (SEQ ID NOS: 207 and 208) and OV83 (SEQ ID NOS: 209 and 210), are all mesothelin markers, and have been found to play a role in cellular adhesion. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thrombasthenia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of neutrophils to sites of extravascular inflammation), disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

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OV17 (SEQ ID NOS: 110 and 111), OV18 (SEQ ID NOS: 112 and 111), OV19 (SEQ ID NOS: 113 and 111), OV20 (SEQ ID NOS: 114 and 111), OV21 (SEQ ID NOS: 115 and 111) and OV22 (SEQ ID NOS: 116 and 117) are folate receptors, which are known to be markers of ovarian cancer. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate ovarian disorders (*e.g.*, ovarian cyst, ovarian fibroma, ovarian endometriosis, ovarian teratoma). Although these markers have been previously associated with ovarian cancer, the expression of such markers has not yet been identified in combination with the expression of other markers including those of the present invention. Such combination of markers will provide improved methods of diagnosing, characterizing, managing and treating ovarian cancer.

OV66 (SEQ ID NOS: 54 and 55), OV7 (SEQ ID NOS: 56 and 57), OV8 (SEQ ID NOS: 58 and 59) and OV81 (SEQ ID NOS: 60 and 61) are ceruloplasmin markers, known to encode a plasma metalloprotein that binds copper in the plasma. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders in blood haemostasis and diseases caused by such an imbalance *e.g.*, (1) cardiovascular diseases or disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cardiomyopathy); (2) neuronal diseases such as Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis; and (3) Wilson's Disease.



**TABLE 1**

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
OV1	ABCB1: ATP-binding cassette, sub-family B (MDR/TAP), member 1	1	2	425..4264
M430	ADPRT: ADP-ribosyltransferase	3	4	160..3204
M571	ANXA2: annexin A2, variant 1	5	6	134..1153
M572	ANXA2: annexin A2, variant 2	7	8	50..1069
M573	ANXA4: annexin A4	9	10	74..1039
OV3	AQP5: aquaporin 5	11	12	519..1316
M352	ARHGAP8: Rho GTPase activating protein 8, variant 1	13	14	142..1536
M353	ARHGAP8: Rho GTPase activating protein 8, variant 2	15	16	1..2043
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV5	BICD1: Bicaudal D homolog 1 (Drosophila)	30	31	82..3009
M431	BTG2: BTG family, member 2	32	33	72..548
M432	CADPS: Ca <sup>2+</sup> -dependent activator protein for secretion	34	35	240..4412
M609	CDH1: cadherin 1, type 1, E-cadherin (epithelial)	36	37	125..2773
M433	CDH6: cadherin 6, type 2, K-cadherin	38	39	327..2699
M434	CDKN2A: cyclin-dependent kinase inhibitor 2A	40	41	41..511
OV9	CGN: cingulin	42	43	152..3763
OV6	CHI3L1: cartilage glycoprotein-39	44	45	127..1278
M435	CKMT1: creatine kinase, mitochondrial 1 (ubiquitous)	46	47	164..1417
M604	CLDN10: claudin 10	48	49	36..772
OV10	CLDN16: claudin 16	50	51	69..986
M360	CLDN4: claudin 4	52	53	183..812
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV7	CP: ceruloplasmin (ferroxidase), variant 2	56	57	<1..2561
OV8	CP: ceruloplasmin (ferroxidase), variant 3	58	59	1..3198
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M103	CRABP2: cellular retinoic acid-binding protein 2	62	63	138..554

OV40	DD96: Epithelial protein up-regulated in carcinoma, membrane associated protein 17	64	65	202..546
OV4	DEC2: basic helix-loop-helix protein	66	67	135..1583
M575	dehydrogenase	68	69	339..1364
M436	DLX5: distal-less homeo box 5	70	71	204..1073
OV12	EAB1: Eab1 protein	72	73	<1..1305
OV13	ESX protein	74	75	96..1211
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M437	FLJ10546: hypothetical protein FLJ10546	84	85	28..1815
OV28	FLJ12799: hypothetical protein FLJ12799	86	87	39..797
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M438	FLJ13782: hypothetical protein FLJ13782	90	91	13..1890
OV29	FLJ20150: hypothetical protein FLJ20150	92	93	78..983
M439	FLJ20327: hypothetical protein FLJ20327	94	95	306..2186
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M442	FLJ20758: hypothetical protein FLJ20758, variant 3	100	101	465..1307
M443	FLJ22252: likely ortholog of mouse SRY-box containing gene 17	102	103	205..1449
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
M400	FLJ22418: hypothetical protein FLJ22418	106	107	71..919
M445	FLJ23499: hypothetical protein FLJ23499	108	109	21..473
OV17	FOLR1: folate receptor 1 (alpha), variant 1	110	111	139..912
OV18	FOLR1: folate receptor 1 (alpha), variant 2	112	111	211..984
OV19	FOLR1: folate receptor 1 (alpha), variant 3	113	111	46..819
OV20	FOLR1: folate receptor 1 (alpha), variant 4	114	111	437..1210
OV21	FOLR1: folate receptor 1 (alpha), variant 5	115	111	11..784
OV22	FOLR3: folate receptor 3 (gamma)	116	117	57..788
OV23	GPR39: G protein-coupled receptor 39	118	119	1..1362
M446	GPRC5B: G protein-coupled receptor, family C, group 5, member B	120	121	109..1320
OV24	G-protein coupled receptor	122	123	274..1236
M447	GRB7: growth factor receptor-bound protein 7	124	125	220..1818
OV11	HAIK1: type I intermediate filament cyto keratin	126	127	61..1329
M448	HOXB7: homeo box B7	128	129	100..753
M138	HSECP1: secretory protein, variant 1	130	131	27..863
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
M451	HSNFRK: HSNFRK protein	136	137	642..2939
OV26	hypothetical protein (1)	138	139	<1..1140
OV27	hypothetical protein (2)	140	141	242..1483
OV31	IFI30: interferon, gamma-inducible protein 30	142	143	41..952
OV58	IGF2: somatomedin A	144	145	553..1095

M452	IMP-2: IGF-II mRNA-binding protein 2	146	147	436..2106
M453	INDO: indoleamine-pyrrole 2, 3 dioxygenase	148	149	23..1234
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M454	ITGA3: integrin, alpha 3	154	155	74..3274
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV34	KIAA0762: KIAA0762 protein	158	159	<1..1875
M455	KIAA0869: KIAA0869 protein	160	161	<1..2668
OV35	KIAA1154: KIAA1154 protein	162	163	<1..677
OV36	KIAA1456: KIAA1456 protein	164	165	<366..1631
OV32	KLK10: kallikrein 10	166	167	82..912
OV33	KLK6: kallikrein 6	168	169	246..980
M456	KRT7: keratin 7, variant 1	170	171	57..1466
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV53	LC27: Putative integral membrane transporter	174	175	204..1055
OV37	LCN2: Lipocalin 2 (oncogene 24p3)	176	177	1..597
M457	LEFTB: left-right determination, factor B	178	179	71..1171
M559	LPHB: lipophilin B (uteroglobin family member), prostatein-like	180	181	64..336
OV38	LYST-interacting protein LIP6	182	183	11..586
OV39	MEIS1: MEIS1 protein	184	185	66..1238
M458	MGB2: mammaglobin 2	186	187	65..352
M459	MGC3184: similar to sialyltransferase 7 ((alpha-N-acetylneuraminy) 2, 3-betagalactosyl-1, 3)-N-acetyl galactosaminide alpha-2, 6-sialyltransferase) E	188	189	176..1186
OV52	MMP7: Matrix metalloproteinase 7 (matrilysin, uterine)	190	191	28..831
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV41	MSLN: mesothelin, variant 6	202	203	<1..>1195
OV42	MSLN: mesothelin, variant 7	204	205	85..1953
OV43	MSLN: mesothelin, variant 8	206	205	88..1956
OV44	MSLN: mesothelin, variant 9	207	208	89..1975
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
OV45	MUC1: mucin 1	211	212	58..1605
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M461	MUC16: mucin 16, variant 2	215	216	25..3471
M612	MUC16: mucin 16, variant 3	215	217	<1..5673
M462	MYOM2: myomesin (M-protein)	218	219	49..4446
M463	NaPi-1ib: sodium dependent phosphate transporter isoform	220	221	36..2105
M464	NME5: protein expressed in non-metastatic cells 5	222	223	15..653

OV47	NUFIP1: nuclear fragile X mental retardation protein interacting protein 1	224	225	1..1488
OV48	OPN-a: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	226	227	1..942
OV49	OPN-b: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	228	229	88..990
OV50	OPN-c: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	230	231	1..861
M578	PAEP: progesterone-associated endometrial protein, variant 1	232	233	36..578
M579	PAEP: progesterone-associated endometrial protein, variant 2	234	233	36..578
M580	PAEP: progesterone-associated endometrial protein, variant 3	235	233	36..578
M581	PAEP: progesterone-associated endometrial protein, variant 4	236	233	36..578
M583	PAEP: progesterone-associated endometrial protein, variant 5	237	238	45..305
M582	PAEP: progesterone-associated endometrial protein, variant 6	239	240	45..521
M613	PAEP: progesterone-associated endometrial protein, variant 7	239	241	45..521
M465	PAX8: paired box gene 8, isoform 8A	242	243	11..1363
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
M470	PRAME: preferentially expressed antigen in melanoma	253	254	236..1765
M615	PRKCI: protein kinase C, iota	255	256	205..1968
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV80	PRSS8: prostatic	261	262	229..1260
OV51	PTGS1: prostaglandin-endoperoxide synthase 1	263	264	6..1805
M312	PTK9: protein tyrosine kinase 9	265	266	61..1113
OV54	pyruvate dehydrogenase complex component E2	267	268	49..>358
OV55	S100A1: S100 calcium-binding protein A1	269	270	114..398
M471	S100A11: S100 calcium-binding protein A11 (calgizzarin)	271	272	121..438
M68	S100A2: S100 calcium-binding protein A2	273	274	41..334
M585	S100A6: S100 calcium-binding protein A6 (calcyclin)	275	276	103..375

OV57	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 1	277	278	100..2109
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M472	secreted protein (HETKL27)	281	282	88..618
M473	SEMA3A: sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	283	284	16..2331
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M586	Similar to proteasome (prosome, macropain) subunit, alpha type, 3	289	290	45..791
M587	Similar to zinc finger protein 136	291	292	139..1524
M475	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 1	293	294	271..447
M185	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 2	295	296	19..417
OV60	SNCG: synuclein, gamma	297	298	49..432
OV59	SORL1: sortilin-related receptor	299	300	198..6842
OV56	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 1	301	302	301..1059
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
OV65	SPON1: VSGP/F-spondin, variant 1	305	306	25..2448
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matriptase	311	312	209..2557
M476	TACSTD2: tumor-associated calcium signal transducer 2	313	314	616..1587
M588	TFPI2: tissue factor pathway inhibitor 2	315	316	57..764
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M328	TSPAN-1: Tetraspan NET-1 protein, variant 2	325	326	1..726
OV46	TTID: myotilin	327	328	281..1777
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV63	unnamed gene (1)	331	332	71..919
OV64	unnamed gene (2)	333	334	28..804
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004

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M479	unnamed gene (9), variant 4	354	355	246..1049
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404
OV25	WFDC2: Epididymis-specific, whey-acidic protein type, four-disulfide core; putative ovarian carcinoma marker	360	361	28..405
M480	XRCC5, KU80: ATP-dependant DNA helicase II	362	363	34..2232

**TABLE 2**

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M575	dehydrogenase	68	69	339..1364
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M583	PAEP: progesterone-associated endometrial protein, variant 5	237	238	45..305

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M613	PAEP: progesterone-associated endometrial protein, variant 7	239	241	45..521
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M475	SLPI: secretory leukocyte protease inhibitor (antileukoprotease), variant 1	293	294	271..447
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matrilysin	311	312	209..2557
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004
M479	unnamed gene (9), variant 4	354	355	246..1049

TABLE 3

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M604	CLDN10: claudin 10	48	49	36..772
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV43	MSLN: mesothelin, variant 8	206	205	88..1956

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M581	PAEP: progestagen-associated endometrial protein, variant 4	236	233	36..578
M582	PAEP: progestagen-associated endometrial protein, variant 6	239	240	45..521
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404

### Definitions

As used herein, each of the following terms has the meaning associated  
 5 with it in this section.

The articles "a" and "an" are used herein to refer to one or to more than one (*i.e.* to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

A "marker" is a gene whose altered level of expression in a tissue or cell  
 10 from its expression level in normal or healthy tissue or cell is associated with a disease state, such as cancer. A "marker nucleic acid" is a nucleic acid (*e.g.*, mRNA, cDNA) encoded by or corresponding to a marker of the invention. Such marker nucleic acids can be DNA (*e.g.*, cDNA) comprising the sequences listed in Table 1 or the complement of such sequences. The marker nucleic acids also can be RNA comprising the  
 15 sequences listed in Table 1 or the complement of such sequence, wherein all thymidine residues are replaced with uridine residues. A "marker protein" is a protein encoded by or corresponding to a marker of the invention. A marker protein comprises the sequence of any of the sequences listed in Table 1. The terms "protein" and "polypeptide" are used interchangeably.

20 The term "probe" refers to any molecule which is capable of selectively binding to a specifically intended target molecule, for example, a nucleotide transcript or protein encoded by or corresponding to a marker. Probes can be either synthesized by one skilled in the art, or derived from appropriate biological preparations. For purposes of detection of the target molecule, probes may be specifically designed to be



labeled, as described herein. Examples of molecules that can be utilized as probes include, but are not limited to, RNA, DNA, proteins, antibodies, and organic molecules.

An "ovary-associated" body fluid is a fluid which, when in the body of a patient, contacts or passes through ovarian cells or into which cells or proteins shed from  
5 ovarian cells *e.g.* ovarian epithelium, are capable of passing. Exemplary ovary-associated body fluids include blood fluids, lymph, ascites, gynecological fluids, cystic fluid, urine, and fluids collected by peritoneal rinsing.

The "normal" level of expression of a marker is the level of expression of the marker in ovarian cells of a human subject or patient not afflicted with ovarian  
10 cancer

An "over-expression" or "significantly higher level of expression" of a marker refers to an expression level in a test sample that is greater than the standard error of the assay employed to assess expression, and is preferably at least twice, and more preferably three, four, five or ten times the expression level of the marker in a  
15 control sample (*e.g.*, sample from a healthy subjects not having the marker associated disease) and preferably, the average expression level of the marker in several control samples.

As used herein, the term "promoter/regulatory sequence" means a nucleic acid sequence which is required for expression of a gene product operably linked to the  
20 promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue-specific manner.

25 A "constitutive" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell under most or all physiological conditions of the cell.

An "inducible" promoter is a nucleotide sequence which, when operably  
30 linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only when an inducer which corresponds to the promoter is present in the cell.

A "tissue-specific" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

5 A "transcribed polynucleotide" or "nucleotide transcript" is a polynucleotide (*e.g.* an mRNA, hnRNA, a cDNA, or an analog of such RNA or cDNA) which is complementary to or homologous with all or a portion of a mature mRNA made by transcription of a marker of the invention and normal post-transcriptional processing (*e.g.* splicing), if any, of the RNA transcript, and reverse transcription of the  
10 RNA transcript.

"Complementary" refers to the broad concept of sequence complementarity between regions of two nucleic acid strands or between two regions of the same nucleic acid strand. It is known that an adenine residue of a first nucleic acid region is capable of forming specific hydrogen bonds ("base pairing") with a residue of  
15 a second nucleic acid region which is antiparallel to the first region if the residue is thymine or uracil. Similarly, it is known that a cytosine residue of a first nucleic acid strand is capable of base pairing with a residue of a second nucleic acid strand which is antiparallel to the first strand if the residue is guanine. A first region of a nucleic acid is complementary to a second region of the same or a different nucleic acid if, when the  
20 two regions are arranged in an antiparallel fashion, at least one nucleotide residue of the first region is capable of base pairing with a residue of the second region. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, when the first and second portions are arranged in an antiparallel fashion, at least about 50%, and preferably at least about 75%, at least about 90%, or at  
25 least about 95% of the nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion. More preferably, all nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion.

"Homologous" as used herein, refers to nucleotide sequence similarity  
30 between two regions of the same nucleic acid strand or between regions of two different nucleic acid strands. When a nucleotide residue position in both regions is occupied by the same nucleotide residue, then the regions are homologous at that position. A first

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region is homologous to a second region if at least one nucleotide residue position of each region is occupied by the same residue. Homology between two regions is expressed in terms of the proportion of nucleotide residue positions of the two regions that are occupied by the same nucleotide residue. By way of example, a region having  
5 the nucleotide sequence 5'-ATTGCC-3' and a region having the nucleotide sequence 5'-TATGGC-3' share 50% homology. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, at least about 50%, and preferably at least about 75%, at least about 90%, or at least about 95% of the nucleotide residue positions of each of the portions are occupied by the same nucleotide residue.  
10 More preferably, all nucleotide residue positions of each of the portions are occupied by the same nucleotide residue.

A molecule is "fixed" or "affixed" to a substrate if it is covalently or non-covalently associated with the substrate such the substrate can be rinsed with a fluid (e.g. standard saline citrate, pH 7.4) without a substantial fraction of the molecule  
15 dissociating from the substrate.

As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in an organism found in nature.

A cancer is "inhibited" if at least one symptom of the cancer is alleviated,  
20 terminated, slowed, or prevented. As used herein, ovarian cancer is also "inhibited" if recurrence or metastasis of the cancer is reduced, slowed, delayed, or prevented.

A kit is any manufacture (e.g. a package or container) comprising at least one reagent, e.g. a probe, for specifically detecting the expression of a marker of the invention. The kit may be promoted, distributed, or sold as a unit for performing the  
25 methods of the present invention.

"Proteins of the invention" encompass marker proteins and their fragments; variant marker proteins and their fragments; peptides and polypeptides comprising an at least 15 amino acid segment of a marker or variant marker protein; and fusion proteins comprising a marker or variant marker protein, or an at least 15 amino  
30 acid segment of a marker or variant marker protein.

Unless otherwise specified herewithin, the terms “antibody” and “antibodies” broadly encompass naturally-occurring forms of antibodies (*e.g.*, IgG, IgA, IgM, IgE) and recombinant antibodies such as single-chain antibodies, chimeric and humanized antibodies and multi-specific antibodies, as well as fragments and derivatives of all of the foregoing, which fragments and derivatives have at least an antigenic binding site. Antibody derivatives may comprise a protein or chemical moiety conjugated to an antibody moiety.

#### Description

The present invention is based, in part, on newly identified markers which are over-expressed in ovarian cancer cells as compared to their expression in normal (*i.e.* non-cancerous) ovarian cells. The enhanced expression of one or more of these markers in ovarian cells is herein correlated with the cancerous state of the tissue. The invention provides compositions, kits, and methods for assessing the cancerous state of ovarian cells (*e.g.* cells obtained from a human, cultured human cells, archived or preserved human cells and *in vivo* cells) as well as treating patients afflicted with ovarian cancer.

The compositions, kits, and methods of the invention have the following uses, among others:

- 1) assessing whether a patient is afflicted with ovarian cancer;
- 2) assessing the stage of ovarian cancer in a human patient;
- 3) assessing the grade of ovarian cancer in a patient;
- 4) assessing the benign or malignant nature of ovarian cancer in a patient;
- 5) assessing the metastatic potential of ovarian cancer in a patient;
- 6) assessing the histological type of neoplasm (*e.g.* serous, mucinous, endometrioid, or clear cell neoplasm) associated with ovarian cancer in a patient;
- 7) making antibodies, antibody fragments or antibody derivatives that are useful for treating ovarian cancer and/or assessing whether a patient is afflicted with ovarian cancer;

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- 8) assessing the presence of ovarian cancer cells;
- 9) assessing the efficacy of one or more test compounds for inhibiting ovarian cancer in a patient;
- 10) assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient;
- 11) monitoring the progression of ovarian cancer in a patient;
- 12) selecting a composition or therapy for inhibiting ovarian cancer in a patient;
- 13) treating a patient afflicted with ovarian cancer;
- 14) inhibiting ovarian cancer in a patient;
- 15) assessing the ovarian carcinogenic potential of a test compound; and
- 16) preventing the onset of ovarian cancer in a patient at risk for developing ovarian cancer.

The invention thus includes a method of assessing whether a patient is afflicted with ovarian cancer which includes assessing whether the patient has pre-metastasized ovarian cancer. This method comprises comparing the level of expression of a marker of the invention (listed in Table 1) in a patient sample and the normal level of expression of the marker in a control, *e.g.*, a non-ovarian cancer sample. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

Gene delivery vehicles, host cells and compositions (all described herein) containing nucleic acids comprising the entirety, or a segment of 15 or more nucleotides, of any of the sequences listed in Tables 1-3 or the complement of such sequences, and polypeptides comprising the entirety, or a segment of 10 or more amino acids, of any of the sequences listed in Tables 1-3 are also provided by this invention.

As described herein, ovarian cancer in patients is associated with an increased level of expression of one or more markers of the invention. While, as discussed above, some of these changes in expression level result from occurrence of the ovarian cancer, others of these changes induce, maintain, and promote the cancerous state of ovarian cancer cells. Thus, ovarian cancer characterized by an increase in the level of expression of one or more markers of the invention can be inhibited by reducing

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and/or interfering with the expression of the markers and/or function of the proteins encoded by those markers.

Expression of a marker of the invention can be inhibited in a number of ways generally known in the art. For example, an antisense oligonucleotide can be  
5 provided to the ovarian cancer cells in order to inhibit transcription, translation, or both, of the marker(s). Alternately, a polynucleotide encoding an antibody, an antibody derivative, or an antibody fragment which specifically binds a marker protein, and operably linked with an appropriate promoter/regulator region, can be provided to the cell in order to generate intracellular antibodies which will inhibit the function or  
10 activity of the protein. The expression and/or function of a marker may also be inhibited by treating the ovarian cancer cell with an antibody, antibody derivative or antibody fragment that specifically binds a marker protein. Using the methods described herein, a variety of molecules, particularly including molecules sufficiently small that they are able to cross the cell membrane, can be screened in order to identify molecules which  
15 inhibit expression of a marker or inhibit the function of a marker protein. The compound so identified can be provided to the patient in order to inhibit ovarian cancer cells of the patient.

Any marker or combination of markers of the invention, as well as any known markers in combination with the markers of the invention, may be used in the  
20 compositions, kits, and methods of the present invention. In general, it is preferable to use markers for which the difference between the level of expression of the marker in ovarian cancer cells and the level of expression of the same marker in normal ovarian cells is as great as possible. Although this difference can be as small as the limit of detection of the method for assessing expression of the marker, it is preferred that the  
25 difference be at least greater than the standard error of the assessment method, and preferably a difference of at least 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 15-, 20-, 25-, 100-, 500-, 1000-fold or greater than the level of expression of the same marker in normal ovarian tissue.

It is recognized that certain marker proteins are secreted from ovarian  
30 cells (*i.e.* one or both of normal and cancerous cells) to the extracellular space surrounding the cells. These markers are preferably used in certain embodiments of the compositions, kits, and methods of the invention, owing to the fact that the such marker

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proteins can be detected in an ovary-associated body fluid sample, which may be more easily collected from a human patient than a tissue biopsy sample. In addition, preferred *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein. For example, the antibody can be labeled  
5 with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

It is a simple matter for the skilled artisan to determine whether any particular marker protein is a secreted protein. In order to make this determination, the marker protein is expressed in, for example, a mammalian cell, preferably a human  
10 ovarian cell line, extracellular fluid is collected, and the presence or absence of the protein in the extracellular fluid is assessed (*e.g.* using a labeled antibody which binds specifically with the protein).

The following is an example of a method which can be used to detect secretion of a protein. About  $8 \times 10^5$  293T cells are incubated at 37°C in wells  
15 containing growth medium (Dulbecco's modified Eagle's medium {DMEM} supplemented with 10% fetal bovine serum) under a 5% (v/v) CO<sub>2</sub>, 95% air atmosphere to about 60-70% confluence. The cells are then transfected using a standard transfection mixture comprising 2 micrograms of DNA comprising an expression vector encoding the protein and 10 microliters of LipofectAMINE™ (GIBCO/BRL Catalog no. 18342-  
20 012) per well. The transfection mixture is maintained for about 5 hours, and then replaced with fresh growth medium and maintained in an air atmosphere. Each well is gently rinsed twice with DMEM which does not contain methionine or cysteine (DMEM-MC; ICN Catalog no. 16-424- 54). About 1 milliliter of DMEM-MC and about 50 microcuries of Trans-<sup>35</sup>S™ reagent (ICN Catalog no. 51006) are added to each  
25 well. The wells are maintained under the 5% CO<sub>2</sub> atmosphere described above and incubated at 37°C for a selected period. Following incubation, 150 microliters of conditioned medium is removed and centrifuged to remove floating cells and debris. The presence of the protein in the supernatant is an indication that the protein is secreted.

Examples of ovary-associated body fluids include blood fluids (*e.g.* whole blood, blood serum, blood having platelets removed therefrom, etc.), lymph, ascitic fluids, gynecological fluids (*e.g.* ovarian, fallopian, and uterine secretions, menses, vaginal douching fluids, fluids used to rinse ovarian cell samples, etc.), cystic  
5 fluid, urine, and fluids collected by peritoneal rinsing (*e.g.* fluids applied and collected during laparoscopy or fluids instilled into and withdrawn from the peritoneal cavity of a human patient). In these embodiments, the level of expression of the marker can be assessed by assessing the amount (*e.g.* absolute amount or concentration) of the marker protein in an ovary-associated body fluid obtained from a patient. The fluid can, of  
10 course, be subjected to a variety of well-known post-collection preparative and storage techniques (*e.g.* storage, freezing, ultrafiltration, concentration, evaporation, centrifugation, etc.) prior to assessing the amount of the marker in the fluid.

Many ovary-associated body fluids (*i.e.* usually excluding urine) can have ovarian cells, *e.g.* ovarian epithelium, therein, particularly when the ovarian cells  
15 are cancerous, and, more particularly, when the ovarian cancer is metastasizing. Cell-containing fluids which can contain ovarian cancer cells include, but are not limited to, peritoneal ascites, fluids collected by peritoneal rinsing, fluids collected by uterine rinsing, uterine fluids such as uterine exudate and menses, pleural fluid, and ovarian exudates. Thus, the compositions, kits, and methods of the invention can be used to  
20 detect expression of marker proteins having at least one portion which is displayed on the surface of cells which express it. It is a simple matter for the skilled artisan to determine whether a marker protein, or a portion thereof, is exposed on the cell surface. For example, immunological methods may be used to detect such proteins on whole cells, or well known computer-based sequence analysis methods (*e.g.* the SIGNALP  
25 program; Nielsen *et al.*, 1997, *Protein Engineering* 10:1-6) may be used to predict the presence of at least one extracellular domain (*i.e.* including both secreted proteins and proteins having at least one cell-surface domain). Expression of a marker protein having at least one portion which is displayed on the surface of a cell which expresses it may be detected without necessarily lysing the cell (*e.g.* using a labeled antibody which binds  
30 specifically with a cell-surface domain of the protein).



Expression of a marker of the invention may be assessed by any of a wide variety of well known methods for detecting expression of a transcribed nucleic acid or protein. Non-limiting examples of such methods include immunological methods for detection of secreted, cell-surface, cytoplasmic, or nuclear proteins, protein  
5 purification methods, protein function or activity assays, nucleic acid hybridization methods, nucleic acid reverse transcription methods, and nucleic acid amplification methods.

In a preferred embodiment, expression of a marker is assessed using an antibody (*e.g.* a radio-labeled, chromophore-labeled, fluorophore-labeled, or enzyme-  
10 labeled antibody), an antibody derivative (*e.g.* an antibody conjugated with a substrate or with the protein or ligand of a protein-ligand pair {*e.g.* biotin-streptavidin} ), or an antibody fragment (*e.g.* a single-chain antibody, an isolated antibody hypervariable domain, etc.) or derivative which binds specifically with a marker protein or fragment thereof, including a marker protein which has undergone all or a portion of its normal  
15 post-translational modification.

In another preferred embodiment, expression of a marker is assessed by preparing mRNA/cDNA (*i.e.* a transcribed polynucleotide) from cells in a patient sample, and by hybridizing the mRNA/cDNA with a reference polynucleotide which is a complement of a marker nucleic acid, or a fragment thereof. cDNA can, optionally, be  
20 amplified using any of a variety of polymerase chain reaction methods prior to hybridization with the reference polynucleotide; preferably, it is not amplified. Expression of one or more markers can likewise be detected using quantitative PCR to assess the level of expression of the marker(s). Alternatively, any of the many known methods of detecting mutations or variants (*e.g.* single nucleotide polymorphisms, deletions, etc.) of a marker of the invention may be used to detect occurrence of a  
25 marker in a patient.

In a related embodiment, a mixture of transcribed polynucleotides obtained from the sample is contacted with a substrate having fixed thereto a polynucleotide complementary to or homologous with at least a portion (*e.g.* at least 7,  
30 10, 15, 20, 25, 30, 40, 50, 100, 500, or more nucleotide residues) of a marker nucleic acid. If polynucleotides complementary to or homologous with several marker nucleic acids are differentially detectable on the substrate (*e.g.* detectable using different

chromophores or fluorophores, or fixed to different selected positions), then the levels of expression of a plurality of markers can be assessed simultaneously using a single substrate (e.g. a "gene chip" microarray of polynucleotides fixed at selected positions). When a method of assessing marker expression is used which involves hybridization of one nucleic acid with another, it is preferred that the hybridization be performed under stringent hybridization conditions.

Because the compositions, kits, and methods of the invention rely on detection of a difference in expression levels of one or more markers of the invention, it is preferable that the level of expression of the marker is significantly greater than the minimum detection limit of the method used to assess expression in at least one of normal ovarian cells and cancerous ovarian cells.

It is understood that by routine screening of additional patient samples using one or more of the markers of the invention, it will be realized that certain of the markers are over-expressed in cancers of various types, including specific ovarian cancers, as well as other cancers such as breast cancer, cervical cancer, etc. For example, it will be confirmed that some of the markers of the invention are over-expressed in most (i.e. 50% or more) or substantially all (i.e. 80% or more) of ovarian cancer. Furthermore, it will be confirmed that certain of the markers of the invention are associated with ovarian cancer of various stages (i.e. stage I, II, III, and IV ovarian cancers, as well as subclassifications IA, IB, IC, IIA, IIB, IIC, IIIA, IIIB, and IIIC, using the FIGO Stage Grouping system for primary carcinoma of the ovary; 1987, *Am. J. Obstet. Gynecol.* 156:236), of various histologic subtypes (e.g. serous, mucinous, endometrioid, and clear cell subtypes, as well as subclassifications and alternate classifications adenocarcinoma, papillary adenocarcinoma, papillary cystadenocarcinoma, surface papillary carcinoma, malignant adenofibroma, cystadenofibroma, adenocarcinoma, cystadenocarcinoma, adenoacanthoma, endometrioid stromal sarcoma, mesodermal (Müllerian) mixed tumor, mesonephroid tumor, malignant carcinoma, Brenner tumor, mixed epithelial tumor, and undifferentiated carcinoma, using the WHO/FIGO system for classification of malignant ovarian tumors; Scully, *Atlas of Tumor Pathology*, 3d series, Washington DC), and various grades (i.e. grade I {well differentiated}, grade II {moderately well differentiated}, and grade III {poorly differentiated from surrounding normal tissue}).

In addition, as a greater number of patient samples are assessed for expression of the markers of the invention and the outcomes of the individual patients from whom the samples were obtained are correlated, it will also be confirmed that increased expression of certain of the markers of the invention are strongly correlated with malignant cancers and that increased expression of other markers of the invention are strongly correlated with benign tumors. The compositions, kits, and methods of the invention are thus useful for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in patients. In addition, these compositions, kits, and methods can be used to detect and differentiate epithelial, stromal, and germ cell ovarian cancers.

When the compositions, kits, and methods of the invention are used for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in a patient, it is preferred that the marker or panel of markers of the invention is selected such that a positive result is obtained in at least about 20%, and preferably at least about 40%, 60%, or 80%, and more preferably in substantially all patients afflicted with an ovarian cancer of the corresponding stage, grade, histological type, or benign/malignant nature. Preferably, the marker or panel of markers of the invention is selected such that a PPV of greater than about 10% is obtained for the general population (more preferably coupled with an assay specificity greater than 99.5%).

When a plurality of markers of the invention are used in the compositions, kits, and methods of the invention, the level of expression of each marker in a patient sample can be compared with the normal level of expression of each of the plurality of markers in non-cancerous samples of the same type, either in a single reaction mixture (*i.e.* using reagents, such as different fluorescent probes, for each marker) or in individual reaction mixtures corresponding to one or more of the markers. In one embodiment, a significantly increased level of expression of more than one of the plurality of markers in the sample, relative to the corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. When a plurality of markers is used, it is preferred that 2, 3, 4, 5, 8, 10, 12, 15, 20, 30, or 50 or more individual markers be used, wherein fewer markers are preferred.

In order to maximize the sensitivity of the compositions, kits, and methods of the invention (*i.e.* by interference attributable to cells of non-ovarian origin in a patient sample), it is preferable that the marker of the invention used therein be a marker which has a restricted tissue distribution, *e.g.*, normally not expressed in a non-epithelial tissue, and more preferably a marker which is normally not expressed in a non-ovarian tissue.

Only a small number of markers are known to be associated with ovarian cancers (*e.g.* *AKT2*, *Ki-RAS*, *ERBB2*, *c-MYC*, *RB1*, and *TP53*; Lynch, *supra*). These markers are not, of course, included among the markers of the invention, although they may be used together with one or more markers of the invention in a panel of markers, for example. It is well known that certain types of genes, such as oncogenes, tumor suppressor genes, growth factor-like genes, protease-like genes, and protein kinase-like genes are often involved with development of cancers of various types. Thus, among the markers of the invention, use of those which correspond to proteins which resemble proteins encoded by known oncogenes and tumor suppressor genes, and those which correspond to proteins which resemble growth factors, proteases, and protein kinases are preferred.

It is recognized that the compositions, kits, and methods of the invention will be of particular utility to patients having an enhanced risk of developing ovarian cancer and their medical advisors. Patients recognized as having an enhanced risk of developing ovarian cancer include, for example, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene (*i.e.* at least one allele), and patients of advancing age (*i.e.* women older than about 50 or 60 years).

The level of expression of a marker in normal (*i.e.* non-cancerous) human ovarian tissue can be assessed in a variety of ways. In one embodiment, this normal level of expression is assessed by assessing the level of expression of the marker in a portion of ovarian cells which appears to be non-cancerous and by comparing this normal level of expression with the level of expression in a portion of the ovarian cells which is suspected of being cancerous. For example, when laparoscopy or other medical procedure, reveals the presence of a lump on one portion of a patient's ovary, but not on another portion of the same ovary or on the other ovary, the normal level of expression of a marker may be assessed using one or both or the non-affected ovary and

a non-affected portion of the affected ovary, and this normal level of expression may be compared with the level of expression of the same marker in an affected portion (*i.e.* the lump) of the affected ovary. Alternately, and particularly as further information becomes available as a result of routine performance of the methods described herein,  
5 population-average values for normal expression of the markers of the invention may be used. In other embodiments, the 'normal' level of expression of a marker may be determined by assessing expression of the marker in a patient sample obtained from a non-cancer-afflicted patient, from a patient sample obtained from a patient before the suspected onset of ovarian cancer in the patient, from archived patient samples, and the  
10 like.

The invention includes compositions, kits, and methods for assessing the presence of ovarian cancer cells in a sample (*e.g.* an archived tissue sample or a sample obtained from a patient). These compositions, kits, and methods are substantially the same as those described above, except that, where necessary, the compositions, kits, and  
15 methods are adapted for use with samples other than patient samples. For example, when the sample to be used is a paraffinized, archived human tissue sample, it can be necessary to adjust the ratio of compounds in the compositions of the invention, in the kits of the invention, or the methods used to assess levels of marker expression in the sample. Such methods are well known in the art and within the skill of the ordinary  
20 artisan.

The invention includes a kit for assessing the presence of ovarian cancer cells (*e.g.* in a sample such as a patient sample). The kit comprises a plurality of reagents, each of which is capable of binding specifically with a marker nucleic acid or protein. Suitable reagents for binding with a marker protein include antibodies,  
25 antibody derivatives, antibody fragments, and the like. Suitable reagents for binding with a marker nucleic acid (*e.g.* a genomic DNA, an mRNA, a spliced mRNA, a cDNA, or the like) include complementary nucleic acids. For example, the nucleic acid reagents may include oligonucleotides (labeled or non-labeled) fixed to a substrate, labeled oligonucleotides not bound with a substrate, pairs of PCR primers, molecular  
30 beacon probes, and the like.

The kit of the invention may optionally comprise additional components useful for performing the methods of the invention. By way of example, the kit may comprise fluids (*e.g.* SSC buffer) suitable for annealing complementary nucleic acids or for binding an antibody with a protein with which it specifically binds, one or more  
5 sample compartments, an instructional material which describes performance of a method of the invention, a sample of normal ovarian cells, a sample of ovarian cancer cells, and the like.

The invention also includes a method of making an isolated hybridoma which produces an antibody useful for assessing whether patient is afflicted with an  
10 ovarian cancer. In this method, a protein or peptide comprising the entirety or a segment of a marker protein is synthesized or isolated (*e.g.* by purification from a cell in which it is expressed or by transcription and translation of a nucleic acid encoding the protein or peptide *in vivo* or *in vitro* using known methods). A vertebrate, preferably a mammal such as a mouse, rat, rabbit, or sheep, is immunized using the protein or peptide. The  
15 vertebrate may optionally (and preferably) be immunized at least one additional time with the protein or peptide, so that the vertebrate exhibits a robust immune response to the protein or peptide. Splenocytes are isolated from the immunized vertebrate and fused with an immortalized cell line to form hybridomas, using any of a variety of methods well known in the art. Hybridomas formed in this manner are then screened  
20 using standard methods to identify one or more hybridomas which produce an antibody which specifically binds with the marker protein or a fragment thereof. The invention also includes hybridomas made by this method and antibodies made using such hybridomas.

The invention also includes a method of assessing the efficacy of a test  
25 compound for inhibiting ovarian cancer cells. As described above, differences in the level of expression of the markers of the invention correlate with the cancerous state of ovarian cells. Although it is recognized that changes in the levels of expression of certain of the markers of the invention likely result from the cancerous state of ovarian cells, it is likewise recognized that changes in the levels of expression of other of the  
30 markers of the invention induce, maintain, and promote the cancerous state of those cells. Thus, compounds which inhibit an ovarian cancer in a patient will cause the level of expression of one or more of the markers of the invention to change to a level nearer

the normal level of expression for that marker (*i.e.* the level of expression for the marker in non-cancerous ovarian cells).

This method thus comprises comparing expression of a marker in a first ovarian cell sample and maintained in the presence of the test compound and expression  
5 of the marker in a second ovarian cell sample and maintained in the absence of the test compound. A significantly reduced expression of a marker of the invention in the presence of the test compound is an indication that the test compound inhibits ovarian cancer. The ovarian cell samples may, for example, be aliquots of a single sample of normal ovarian cells obtained from a patient, pooled samples of normal ovarian cells  
10 obtained from a patient, cells of a normal ovarian cell line, aliquots of a single sample of ovarian cancer cells obtained from a patient, pooled samples of ovarian cancer cells obtained from a patient, cells of an ovarian cancer cell line, or the like. In one embodiment, the samples are ovarian cancer cells obtained from a patient and a plurality of compounds known to be effective for inhibiting various ovarian cancers are tested in  
15 order to identify the compound which is likely to best inhibit the ovarian cancer in the patient.

This method may likewise be used to assess the efficacy of a therapy for inhibiting ovarian cancer in a patient. In this method, the level of expression of one or more markers of the invention in a pair of samples (one subjected to the therapy, the  
20 other not subjected to the therapy) is assessed. As with the method of assessing the efficacy of test compounds, if the therapy induces a significantly lower level of expression of a marker of the invention then the therapy is efficacious for inhibiting ovarian cancer. As above, if samples from a selected patient are used in this method, then alternative therapies can be assessed *in vitro* in order to select a therapy most likely  
25 to be efficacious for inhibiting ovarian cancer in the patient.

As described above, the cancerous state of human ovarian cells is correlated with changes in the levels of expression of the markers of the invention. The invention includes a method for assessing the human ovarian cell carcinogenic potential of a test compound. This method comprises maintaining separate aliquots of human  
30 ovarian cells in the presence and absence of the test compound. Expression of a marker of the invention in each of the aliquots is compared. A significantly higher level of expression of a marker of the invention in the aliquot maintained in the presence of the

test compound (relative to the aliquot maintained in the absence of the test compound) is an indication that the test compound possesses human ovarian cell carcinogenic potential. The relative carcinogenic potentials of various test compounds can be assessed by comparing the degree of enhancement or inhibition of the level of  
5 expression of the relevant markers, by comparing the number of markers for which the level of expression is enhanced or inhibited, or by comparing both.

Various aspects of the invention are described in further detail in the following subsections.

#### 10 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules, including nucleic acids which encode a marker protein or a portion thereof. Isolated nucleic acids of the invention also include nucleic acid molecules sufficient for use as hybridization probes to identify marker nucleic acid molecules, and fragments of marker  
15 nucleic acid molecules, *e.g.*, those suitable for use as PCR primers for the amplification or mutation of marker nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA) and RNA molecules (*e.g.*, mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-  
20 stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Preferably, an "isolated" nucleic acid molecule is free of sequences (preferably protein-encoding sequences) which naturally flank the nucleic acid (*i.e.*,  
25 sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kB, 4 kB, 3 kB, 2 kB, 1 kB, 0.5 kB or 0.1 kB of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover,  
30 an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques,



or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention can be isolated using standard molecular biology techniques and the sequence information in the database records described herein. Using all or a portion of such nucleic acid sequences, nucleic acid molecules of the invention can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook *et al.*, ed., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid molecule of the invention can be amplified using cDNA, mRNA, or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, nucleotides corresponding to all or a portion of a nucleic acid molecule of the invention can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which has a nucleotide sequence complementary to the nucleotide sequence of a marker nucleic acid or to the nucleotide sequence of a nucleic acid encoding a marker protein. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, a nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence, wherein the full length nucleic acid sequence comprises a marker nucleic acid or which encodes a marker protein. Such nucleic acids can be used, for example, as a probe or primer. The probe/primer typically is used as one or more substantially purified oligonucleotides. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 7, preferably about 15, more preferably about 25, 50, 75, 100, 125, 150, 175, 200, 250, 300, 350, or 400 or more consecutive nucleotides of a nucleic acid of the invention.

Probes based on the sequence of a nucleic acid molecule of the invention can be used to detect transcripts or genomic sequences corresponding to one or more markers of the invention. The probe comprises a label group attached thereto, *e.g.*, a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes  
5 can be used as part of a diagnostic test kit for identifying cells or tissues which mis-express the protein, such as by measuring levels of a nucleic acid molecule encoding the protein in a sample of cells from a subject, *e.g.*, detecting mRNA levels or determining whether a gene encoding the protein has been mutated or deleted.

The invention further encompasses nucleic acid molecules that differ, due  
10 to degeneracy of the genetic code, from the nucleotide sequence of nucleic acids encoding a marker protein and thus encode the same protein.

It will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequence can exist within a population (*e.g.*, the human population). Such genetic polymorphisms can exist among  
15 individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. In addition, it will be appreciated that DNA polymorphisms that affect RNA expression levels can also exist that may affect the overall expression level of that gene (*e.g.*, by affecting regulation or degradation).

20 As used herein, the phrase "allelic variant" refers to a nucleotide sequence which occurs at a given locus or to a polypeptide encoded by the nucleotide sequence.

As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a polypeptide corresponding  
25 to a marker of the invention. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of a given gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid  
30 polymorphisms or variations that are the result of natural allelic variation and that do not alter the functional activity are intended to be within the scope of the invention.

In another embodiment, an isolated nucleic acid molecule of the invention is at least 7, 15, 20, 25, 30, 40, 60, 80, 100, 150, 200, 250, 300, 350, 400, 450, 550, 650, 700, 800, 900, 1000, 1200, 1400, 1600, 1800, 2000, 2200, 2400, 2600, 2800, 3000, 3500, 4000, 4500, or more nucleotides in length and hybridizes under stringent  
5 conditions to a marker nucleic acid or to a nucleic acid encoding a marker protein. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found  
10 in sections 6.3.1-6.3.6 of *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989). A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

In addition to naturally-occurring allelic variants of a nucleic acid  
15 molecule of the invention that can exist in the population, the skilled artisan will further appreciate that sequence changes can be introduced by mutation thereby leading to changes in the amino acid sequence of the encoded protein, without altering the biological activity of the protein encoded thereby. For example, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino  
20 acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are not conserved or only semi-conserved among homologs of various species may be non-essential for activity and thus would be likely targets for alteration.  
25 Alternatively, amino acid residues that are conserved among the homologs of various species (*e.g.*, murine and human) may be essential for activity and thus would not be likely targets for alteration.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding a variant marker protein that contain changes in amino acid residues  
30 that are not essential for activity. Such variant marker proteins differ in amino acid sequence from the naturally-occurring marker proteins, yet retain biological activity. In one embodiment, such a variant marker protein has an amino acid sequence that is at

least about 40% identical, 50%, 60%, 70%, 80%, 90%, 95%, or 98% identical to the amino acid sequence of a marker protein.

An isolated nucleic acid molecule encoding a variant marker protein can be created by introducing one or more nucleotide substitutions, additions or deletions  
5 into the nucleotide sequence of marker nucleic acids, such that one or more amino acid residue substitutions, additions, or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative  
10 amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine,  
15 serine, threonine, tyrosine, cysteine), non-polar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis,  
20 and the resultant mutants can be screened for biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

The present invention encompasses antisense nucleic acid molecules, *i.e.*, molecules which are complementary to a sense nucleic acid of the invention, *e.g.*,  
25 complementary to the coding strand of a double-stranded marker cDNA molecule or complementary to a marker mRNA sequence. Accordingly, an antisense nucleic acid of the invention can hydrogen bond to (*i.e.* anneal with) a sense nucleic acid of the invention. The antisense nucleic acid can be complementary to an entire coding strand, or to only a portion thereof, *e.g.*, all or part of the protein coding region (or open reading  
30 frame). An antisense nucleic acid molecule can also be antisense to all or part of a non-coding region of the coding strand of a nucleotide sequence encoding a marker protein.

The non-coding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 or more nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (*v*), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (*v*), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)*w*, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been sub-cloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a marker protein to thereby inhibit expression of the marker, *e.g.*, by inhibiting transcription and/or translation. The

hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. Examples of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site or infusion of the antisense nucleic acid into an ovary-associated body fluid. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\alpha$ -units, the strands run parallel to each other (Gaultier *et al.*, 1987, *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-O-methylribonucleotide (Inoue *et al.*, 1987, *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.*, 1987, *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach, 1988, *Nature* 334:585-591) can be used to catalytically cleave mRNA transcripts to thereby inhibit translation of the protein encoded by the mRNA. A ribozyme having specificity for a nucleic acid molecule encoding a marker protein can be designed based upon the nucleotide sequence of a cDNA corresponding to the marker. For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved

(see Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742). Alternatively, an mRNA encoding a polypeptide of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see, *e.g.*, Bartel and Szostak, 1993, *Science* 261:1411-1418).

5           The invention also encompasses nucleic acid molecules which form triple helical structures. For example, expression of a marker of the invention can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the gene encoding the marker nucleic acid or protein (*e.g.*, the promoter and/or enhancer) to form triple helical structures that prevent transcription of the gene in target cells. See  
10   generally Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

          In various embodiments, the nucleic acid molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose  
15   phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.*, 1996, *Bioorganic & Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral  
20   backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996), *supra*; Perry-O'Keefe *et al.* (1996) *Proc. Natl. Acad. Sci. USA* 93:14670-675.

25           PNAs can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction  
30   enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup (1996), *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup, 1996, *supra*; Perry-O'Keefe *et al.*, 1996, *Proc. Natl. Acad. Sci. USA* 93:14670-675).

In another embodiment, PNAs can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated  
5 which can combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and  
10 orientation (Hyrup, 1996, *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996), *supra*, and Finn *et al.* (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can  
15 be used as a link between the PNA and the 5' end of DNA (Mag *et al.*, 1989, *Nucleic Acids Res.* 17:5973-88). PNA monomers are then coupled in a step-wise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.*, 1996, *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser *et al.*, 1975,  
20 *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide can include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre *et al.*, 1987, *Proc. Natl. Acad. Sci. USA*  
25 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, *e.g.*, Krol *et al.*, 1988, *Bio/Techniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide can be conjugated to another molecule, *e.g.*, a peptide,  
30 hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.



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The invention also includes molecular beacon nucleic acids having at least one region which is complementary to a nucleic acid of the invention, such that the molecular beacon is useful for quantitating the presence of the nucleic acid of the invention in a sample. A "molecular beacon" nucleic acid is a nucleic acid comprising a pair of complementary regions and having a fluorophore and a fluorescent quencher associated therewith. The fluorophore and quencher are associated with different portions of the nucleic acid in such an orientation that when the complementary regions are annealed with one another, fluorescence of the fluorophore is quenched by the quencher. When the complementary regions of the nucleic acid are not annealed with one another, fluorescence of the fluorophore is quenched to a lesser degree. Molecular beacon nucleic acids are described, for example, in U.S. Patent 5,876,930.

## II. Isolated Proteins and Antibodies

One aspect of the invention pertains to isolated marker proteins and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise antibodies directed against a marker protein or a fragment thereof. In one embodiment, the native marker protein can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, a protein or peptide comprising the whole or a segment of the marker protein is produced by recombinant DNA techniques. Alternative to recombinant expression, such protein or peptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein"). When the protein or biologically active portion thereof is recombinantly produced, it is

also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When the protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of the protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the polypeptide of interest.

Biologically active portions of a marker protein include polypeptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the marker protein, which include fewer amino acids than the full length protein, and exhibit at least one activity of the corresponding full-length protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the corresponding full-length protein. A biologically active portion of a marker protein of the invention can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length. Moreover, other biologically active portions, in which other regions of the marker protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of the native form of the marker protein.

Preferred marker proteins are encoded by nucleotide sequences comprising the sequences listed in Tables 1-3. Other useful proteins are substantially identical (*e.g.*, at least about 40%, preferably 50%, 60%, 70%, 80%, 90%, 95%, or 99%) to one of these sequences and retain the functional activity of the corresponding naturally-occurring marker protein yet differ in amino acid sequence due to natural allelic variation or mutagenesis.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences

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is a function of the number of identical positions shared by the sequences (*i.e.*, % identity = # of identical positions/total # of positions (*e.g.*, overlapping positions)  $\times 100$ ).

In one embodiment the two sequences are the same length.

The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-2268, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the BLASTN and BLASTX programs of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST nucleotide searches can be performed with the BLASTN program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the invention. BLAST protein searches can be performed with the BLASTP program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to a protein molecules of the invention. To obtain gapped alignments for comparison purposes, a newer version of the BLAST algorithm called Gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402, which is able to perform gapped local alignments for the programs BLASTN, BLASTP and BLASTX. Alternatively, PSI-Blast can be used to perform an iterated search which detects distant relationships between molecules. When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, BLASTX and BLASTN) can be used. Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, (1988) *CABIOS* 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Yet another useful algorithm for identifying regions of local sequence similarity and alignment is the FASTA algorithm as described in Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85:2444-2448. When using the FASTA algorithm for comparing nucleotide or amino acid sequences, a PAM120 weight residue table can, for example, be used with a *k*-tuple value of 2.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, only exact matches are counted.

The invention also provides chimeric or fusion proteins comprising a marker protein or a segment thereof. As used herein, a "chimeric protein" or "fusion protein" comprises all or part (preferably a biologically active part) of a marker protein operably linked to a heterologous polypeptide (*i.e.*, a polypeptide other than the marker protein). Within the fusion protein, the term "operably linked" is intended to indicate that the marker protein or segment thereof and the heterologous polypeptide are fused in-frame to each other. The heterologous polypeptide can be fused to the amino-terminus or the carboxyl-terminus of the marker protein or segment.

One useful fusion protein is a GST fusion protein in which a marker protein or segment is fused to the carboxyl terminus of GST sequences. Such fusion proteins can facilitate the purification of a recombinant polypeptide of the invention.

In another embodiment, the fusion protein contains a heterologous signal sequence at its amino terminus. For example, the native signal sequence of a marker protein can be removed and replaced with a signal sequence from another protein. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1992). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the *phoA* secretory signal (Sambrook *et al.*, *supra*) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an immunoglobulin fusion protein in which all or part of a marker protein is fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand (soluble or membrane-bound) and a protein on the surface of a cell (receptor), to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion protein can be used to affect the bioavailability of a

cognate ligand of a marker protein. Inhibition of ligand/receptor interaction can be useful therapeutically, both for treating proliferative and differentiative disorders and for modulating (e.g. promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies  
5 directed against a marker protein in a subject, to purify ligands and in screening assays to identify molecules which inhibit the interaction of the marker protein with ligands.

Chimeric and fusion proteins of the invention can be produced by standard recombinant DNA techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers.  
10 Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see, e.g., Ausubel *et al.*, *supra*). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide).  
15 A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the polypeptide of the invention.

A signal sequence can be used to facilitate secretion and isolation of marker proteins. Signal sequences are typically characterized by a core of hydrophobic  
20 amino acids which are generally cleaved from the mature protein during secretion in one or more cleavage events. Such signal peptides contain processing sites that allow cleavage of the signal sequence from the mature proteins as they pass through the secretory pathway. Thus, the invention pertains to marker proteins, fusion proteins or segments thereof having a signal sequence, as well as to such proteins from which the  
25 signal sequence has been proteolytically cleaved (*i.e.*, the cleavage products). In one embodiment, a nucleic acid sequence encoding a signal sequence can be operably linked in an expression vector to a protein of interest, such as a marker protein or a segment thereof. The signal sequence directs secretion of the protein, such as from a eukaryotic host into which the expression vector is transformed, and the signal sequence is  
30 subsequently or concurrently cleaved. The protein can then be readily purified from the extracellular medium by art recognized methods. Alternatively, the signal sequence can

be linked to the protein of interest using a sequence which facilitates purification, such as with a GST domain.

The present invention also pertains to variants of the marker proteins. Such variants have an altered amino acid sequence which can function as either agonists (mimetics) or as antagonists. Variants can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation. An agonist can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the protein. An antagonist of a protein can inhibit one or more of the activities of the naturally occurring form of the protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the protein of interest. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer side effects in a subject relative to treatment with the naturally occurring form of the protein.

Variants of a marker protein which function as either agonists (mimetics) or as antagonists can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of the protein of the invention for agonist or antagonist activity. In one embodiment, a variegated library of variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential protein sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display). There are a variety of methods which can be used to produce libraries of potential variants of the marker proteins from a degenerate oligonucleotide sequence. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang, 1983, *Tetrahedron* 39:3; Itakura *et al.*, 1984, *Annu. Rev. Biochem.* 53:323; Itakura *et al.*, 1984, *Science* 198:1056; Ike *et al.*, 1983 *Nucleic Acid Res.* 11:477).

In addition, libraries of segments of a marker protein can be used to generate a variegated population of polypeptides for screening and subsequent selection of variant marker proteins or segments thereof. For example, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of the

coding sequence of interest with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by  
5 treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes amino terminal and internal fragments of various sizes of the protein of interest.

Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA  
10 libraries for gene products having a selected property. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates  
15 isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify variants of a protein of the invention (Arkin and Yourvan, 1992, *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave *et al.*, 1993, *Protein Engineering* 6(3):327-331).

20 Another aspect of the invention pertains to antibodies directed against a protein of the invention. In preferred embodiments, the antibodies specifically bind a marker protein or a fragment thereof. The terms "antibody" and "antibodies" as used interchangeably herein refer to immunoglobulin molecules as well as fragments and derivatives thereof that comprise an immunologically active portion of an  
25 immunoglobulin molecule, (*i.e.*, such a portion contains an antigen binding site which specifically binds an antigen, such as a marker protein, *e.g.*, an epitope of a marker protein). An antibody which specifically binds to a protein of the invention is an antibody which binds the protein, but does not substantially bind other molecules in a sample, *e.g.*, a biological sample, which naturally contains the protein. Examples of an  
30 immunologically active portion of an immunoglobulin molecule include, but are not limited to, single-chain antibodies (scAb), F(ab) and F(ab')<sub>2</sub> fragments.

An isolated protein of the invention or a fragment thereof can be used as an immunogen to generate antibodies. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments for use as immunogens. The antigenic peptide of a protein of the invention comprises at least 8 (preferably 10, 15, 20, or 30 or more) amino acid residues of the amino acid sequence of one of the proteins of the invention, and encompasses at least one epitope of the protein such that an antibody raised against the peptide forms a specific immune complex with the protein. Preferred epitopes encompassed by the antigenic peptide are regions that are located on the surface of the protein, *e.g.*, hydrophilic regions. Hydrophobicity sequence analysis, hydrophilicity sequence analysis, or similar analyses can be used to identify hydrophilic regions. In preferred embodiments, an isolated marker protein or fragment thereof is used as an immunogen.

An immunogen typically is used to prepare antibodies by immunizing a suitable (*i.e.* immunocompetent) subject such as a rabbit, goat, mouse, or other mammal or vertebrate. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed or chemically-synthesized protein or peptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or a similar immunostimulatory agent. Preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a protein of the invention. In such a manner, the resulting antibody compositions have reduced or no binding of human proteins other than a protein of the invention.

The invention provides polyclonal and monoclonal antibodies. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope. Preferred polyclonal and monoclonal antibody compositions are ones that have been selected for antibodies directed against a protein of the invention. Particularly preferred polyclonal and monoclonal antibody preparations are ones that contain only antibodies directed against a marker protein or fragment thereof.



Polyclonal antibodies can be prepared by immunizing a suitable subject with a protein of the invention as an immunogen. The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. At an appropriate time after immunization, *e.g.*, when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies (mAb) by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (see Kozbor *et al.*, 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (see Cole *et al.*, pp. 77-96 In *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., 1985) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology*, Coligan *et al.* ed., John Wiley & Sons, New York, 1994). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, *e.g.*, using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a protein of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (*e.g.*, an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (*e.g.*, the Pharmacia *Recombinant Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J.* 12:725-734.

The invention also provides recombinant antibodies that specifically bind a protein of the invention. In preferred embodiments, the recombinant antibodies specifically binds a marker protein or fragment thereof. Recombinant antibodies include, but are not limited to, chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, single-chain antibodies and multi-specific antibodies. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, *e.g.*, Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Single-chain antibodies have an antigen binding site and consist of single polypeptides. They can be produced by techniques known in the art, for example using methods described in Ladner *et. al* U.S. Pat. No. 4,946,778 (which is incorporated herein by reference in its entirety); Bird *et al.*, (1988) *Science* 242:423-426; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:1-9; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:97-105; and Huston *et al.*, (1991) *Methods in Enzymology Molecular Design and Modeling: Concepts and Applications* 203:46-88. Multi-specific antibodies are antibody molecules having at least two antigen-binding sites that specifically bind different antigens. Such molecules can be produced by techniques known in the art, for example using methods described in Segal, U.S. Patent No. 4,676,980 (the disclosure of which is incorporated herein by reference in its entirety); Holliger et al., (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; Whitlow *et al.*, (1994) *Protein Eng.* 7:1017-1026 and U.S. Pat. No. 6,121,424.

Humanized antibodies are antibody molecules from non-human species having one or more complementarity determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, *e.g.*, Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better *et al.* (1988) *Science* 240:1041-1043; Liu *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu

*et al.* (1987) *J. Immunol.* 139:3521- 3526; Sun *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura *et al.* (1987) *Cancer Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.* (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi *et al.* (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones *et al.* (1986) *Nature* 321:552-525; Verhoeyan *et al.* (1988) *Science* 239:1534; and Beidler *et al.* (1988) *J. Immunol.* 141:4053-4060.

More particularly, humanized antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes.

10 The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.*, all or a portion of a polypeptide corresponding to a marker of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class

15 switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995) *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, *e.g.*,

20 U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be

25 generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, *e.g.*, a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope (Jespersen *et al.*, 1994, *Bio/technology* 12:899-903).

The antibodies of the invention can be isolated after production (*e.g.*,

30 from the blood or serum of the subject) or synthesis and further purified by well-known techniques. For example, IgG antibodies can be purified using protein A chromatography. Antibodies specific for a protein of the invention can be selected or

(e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, *i.e.*, one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those of the desired protein of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein of the invention.

In a preferred embodiment, the substantially purified antibodies of the invention may specifically bind to a signal peptide, a secreted sequence, an extracellular domain, a transmembrane or a cytoplasmic domain or cytoplasmic membrane of a protein of the invention. In a particularly preferred embodiment, the substantially purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a protein of the invention. In a more preferred embodiment, the substantially purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a marker protein.

An antibody directed against a protein of the invention can be used to isolate the protein by standard techniques, such as affinity chromatography or immunoprecipitation. Moreover, such an antibody can be used to detect the marker protein or fragment thereof (e.g., in a cellular lysate or cell supernatant) in order to evaluate the level and pattern of expression of the marker. The antibodies can also be used diagnostically to monitor protein levels in tissues or body fluids (e.g. in an ovary-associated body fluid) as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by the

use of an antibody derivative, which comprises an antibody of the invention coupled to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish  
5 peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol;  
10 examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

Antibodies of the invention may also be used as therapeutic agents in treating cancers. In a preferred embodiment, completely human antibodies of the invention are used for therapeutic treatment of human cancer patients, particularly those  
15 having an ovarian cancer. In another preferred embodiment, antibodies that bind specifically to a marker protein or fragment thereof are used for therapeutic treatment. Further, such therapeutic antibody may be an antibody derivative or immunotoxin comprising an antibody conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any  
20 agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof.  
25 Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines  
30 (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine and vinblastine).

The conjugated antibodies of the invention can be used for modifying a given biological response, for the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as ribosome-inhibiting protein (see Better et al., U.S. Patent No. 6,146,631, the disclosure of which is incorporated herein in its entirety), abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, .alpha.-interferon, .beta.-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophase colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, *e.g.*, Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in *Monoclonal Antibodies And Cancer Therapy*, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in *Controlled Drug Delivery* (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in *Monoclonal Antibodies For Cancer Detection And Therapy*, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", *Immunol. Rev.*, 62:119-58 (1982).

Accordingly, in one aspect, the invention provides substantially purified antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. In various embodiments, the substantially purified antibodies of the invention, or fragments or derivatives thereof, can be human, non-human, chimeric and/or humanized antibodies. In another aspect, the invention provides non-human antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. Such non-human antibodies can be goat, mouse, sheep, horse, chicken, rabbit, or rat

antibodies. Alternatively, the non-human antibodies of the invention can be chimeric and/or humanized antibodies. In addition, the non-human antibodies of the invention can be polyclonal antibodies or monoclonal antibodies. In still a further aspect, the invention provides monoclonal antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. The monoclonal antibodies can be human, humanized, chimeric and/or non-human antibodies.

The invention also provides a kit containing an antibody of the invention conjugated to a detectable substance, and instructions for use. Still another aspect of the invention is a pharmaceutical composition comprising an antibody of the invention and a pharmaceutically acceptable carrier. In preferred embodiments, the pharmaceutical composition contains an antibody of the invention, a therapeutic moiety, and a pharmaceutically acceptable carrier.

### 15 III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding a marker protein (or a portion of such a protein). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, namely expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective

retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell.

5 This means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression  
10 of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, *Methods in Enzymology: Gene Expression Technology* vol.185,  
15 Academic Press, San Diego, CA (1991). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the  
20 host cell to be transformed, the level of expression of protein desired, and the like. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein.

The recombinant expression vectors of the invention can be designed for  
25 expression of a marker protein or a segment thereof in prokaryotic (*e.g.*, *E. coli*) or eukaryotic cells (*e.g.*, insect cells {using baculovirus expression vectors}, yeast cells or mammalian cells). Suitable host cells are discussed further in Goeddel, *supra*.

Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

30 Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a



protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification.

- 5 Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX
- 10 (Pharmacia Biotech Inc; Smith and Johnson, 1988, *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

- Examples of suitable inducible non-fusion *E. coli* expression vectors
- 15 include pTrc (Amann *et al.*, 1988, *Gene* 69:301-315) and pET 11d (Studier *et al.*, p. 60-89, In *Gene Expression Technology: Methods in Enzymology* vol.185, Academic Press, San Diego, CA, 1991). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter
- 20 mediated by a co-expressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

- One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave
- 25 the recombinant protein (Gottesman, p. 119-128, In *Gene Expression Technology: Methods in Enzymology* vol. 185, Academic Press, San Diego, CA, 1990. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada *et al.*, 1992, *Nucleic Acids Res.* 20:2111-2118).
- 30 Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1 (Baldari *et al.*, 1987, *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz, 1982, *Cell* 30:933-943), pJRY88 (Schultz *et al.*, 1987, *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and pPicZ (Invitrogen Corp, San Diego, CA).

Alternatively, the expression vector is a baculovirus expression vector. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, Sf 9 cells) include the pAc series (Smith *et al.*, 1983, *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers, 1989, *Virology* 170:31-39).

10 In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987, *Nature* 329:840) and pMT2PC (Kaufman *et al.*, 1987, *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements.

15 For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook *et al.*, *supra*.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type

20 (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert *et al.*, 1987, *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton, 1988, *Adv. Immunol.* 43:235-275), in particular promoters of T cell receptors (Winoto and

25 Baltimore, 1989, *EMBO J.* 8:729-733) and immunoglobulins (Banerji *et al.*, 1983, *Cell* 33:729-740; Queen and Baltimore, 1983, *Cell* 33:741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle, 1989, *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund *et al.*, 1985, *Science* 230:912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Patent No.

30 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters

(Kessel and Gruss, 1990, *Science* 249:374-379) and the  $\alpha$ -fetoprotein promoter (Camper and Tilghman, 1989, *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory  
5 sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to the mRNA encoding a polypeptide of the invention. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the  
10 antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue-specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid, or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency  
15 regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see Weintraub *et al.*, 1986, *Trends in Genetics*, Vol. 1(1).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host  
20 cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term  
25 as used herein.

A host cell can be any prokaryotic (*e.g.*, *E. coli*) or eukaryotic cell (*e.g.*, insect cells, yeast or mammalian cells).

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms  
30 "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection,

lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells  
5 may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.*, for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Cells stably transfected with the introduced nucleic acid  
10 can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce a marker protein or a segment thereof. Accordingly, the invention further provides methods for producing a marker protein or a segment  
15 thereof using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of the invention (into which a recombinant expression vector encoding a marker protein or a segment thereof has been introduced) in a suitable medium such that the is produced. In another embodiment, the method further comprises isolating the a marker protein or a segment thereof from the medium or the  
20 host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which a sequences encoding a marker protein or a segment thereof have been introduced. Such host cells can then be used to  
25 create non-human transgenic animals in which exogenous sequences encoding a marker protein of the invention have been introduced into their genome or homologous recombinant animals in which endogenous gene(s) encoding a marker protein have been altered. Such animals are useful for studying the function and/or activity of the marker protein and for identifying and/or evaluating modulators of marker protein. As used  
30 herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human

primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

10 A transgenic animal of the invention can be created by introducing a nucleic acid encoding a marker protein into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the transgene to direct expression of the polypeptide of the invention to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 15 4,873,191 and in Hogan, *Manipulating the Mouse Embryo*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of mRNA encoding the transgene in tissues or cells of the animals. A transgenic founder animal 20 can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying the transgene can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a gene encoding a marker protein into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous gene is functionally disrupted (i.e., no longer encodes a 30

functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous protein). In the homologous recombination vector, the altered portion of the gene is flanked at its 5' and 3' ends by additional nucleic acid of the gene to allow for homologous recombination to occur between the exogenous gene carried by the vector and an endogenous gene in an embryonic stem cell. The additional flanking nucleic acid sequences are of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, *e.g.*, Thomas and Capecchi, 1987, *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced gene has homologously recombined with the endogenous gene are selected (see, *e.g.*, Li *et al.*, 1992, *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras (see, *e.g.*, Bradley, *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, Ed., IRL, Oxford, 1987, pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication NOS. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, *e.g.*, Lakso *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman *et al.*, 1991, *Science* 251:1351-1355). If a *cre/loxP* recombinase system is used to regulate expression of the

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transgene, animals containing transgenes encoding both the *Cre* recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut *et al.* (1997) *Nature* 385:810-813 and PCT Publication NOS. WO 97/07668 and WO 97/07669.

#### 10 IV. Pharmaceutical Compositions

The nucleic acid molecules, polypeptides, and antibodies (also referred to herein as "active compounds") of the invention can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier.

15 As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

The invention includes methods for preparing pharmaceutical compositions for modulating the expression or activity of a marker nucleic acid or protein. Such methods comprise formulating a pharmaceutically acceptable carrier with an agent which modulates expression or activity of a marker nucleic acid or protein. Such compositions can further include additional active agents. Thus, the invention further includes methods for preparing a pharmaceutical composition by formulating a pharmaceutically acceptable carrier with an agent which modulates expression or activity of a marker nucleic acid or protein and one or more additional active compounds.

The invention also provides methods (also referred to herein as "screening assays") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, peptoids, small molecules or other drugs) which (a) bind to the marker, or (b) have a modulatory (*e.g.*, stimulatory or inhibitory) effect on the activity of the marker or, more specifically, (c) have a modulatory effect on the interactions of the marker with one or more of its natural substrates (*e.g.*, peptide, protein, hormone, co-factor, or nucleic acid), or (d) have a modulatory effect on the expression of the marker. Such assays typically comprise a reaction between the marker and one or more assay components. The other components may be either the test compound itself, or a combination of test compound and a natural binding partner of the marker.

The test compounds of the present invention may be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. Test compounds may also be obtained by any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive; see, *e.g.*, Zuckermann *et al.*, 1994, *J. Med. Chem.* 37:2678-85); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic library methods using affinity chromatography selection. The biological library and peptoid library approaches are limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, 1997, *Anticancer Drug Des.* 12:145).

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt *et al.* (1993) *Proc. Natl. Acad. Sci. U.S.A.* 90:6909; Erb *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:11422; Zuckermann *et al.* (1994). *J. Med. Chem.* 37:2678; Cho *et al.* (1993) *Science* 261:1303; Carrell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and in Gallop *et al.* (1994) *J. Med. Chem.* 37:1233.



Libraries of compounds may be presented in solution (e.g., Houghten, 1992, *Biotechniques* 13:412-421), or on beads (Lam, 1991, *Nature* 354:82-84), chips (Fodor, 1993, *Nature* 364:555-556), bacteria and/or spores, (Ladner, USP 5,223,409), plasmids (Cull *et al*, 1992, *Proc Natl Acad Sci USA* 89:1865-1869) or on phage (Scott  
5 and Smith, 1990, *Science* 249:386-390; Devlin, 1990, *Science* 249:404-406; Cwirla *et al*, 1990, *Proc. Natl. Acad. Sci.* 87:6378-6382; Felici, 1991, *J. Mol. Biol.* 222:301-310; Ladner, *supra*).

In one embodiment, the invention provides assays for screening candidate or test compounds which are substrates of a protein encoded by or  
10 corresponding to a marker or biologically active portion thereof. In another embodiment, the invention provides assays for screening candidate or test compounds which bind to a protein encoded by or corresponding to a marker or biologically active portion thereof. Determining the ability of the test compound to directly bind to a protein can be accomplished, for example, by coupling the compound with a  
15 radioisotope or enzymatic label such that binding of the compound to the marker can be determined by detecting the labeled marker compound in a complex. For example, compounds (e.g., marker substrates) can be labeled with  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ , or  $^3\text{H}$ , either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, assay components can be enzymatically  
20 labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product.

In another embodiment, the invention provides assays for screening candidate or test compounds which modulate the expression of a marker or the activity  
25 of a protein encoded by or corresponding to a marker, or a biologically active portion thereof. In all likelihood, the protein encoded by or corresponding to the marker can, *in vivo*, interact with one or more molecules, such as but not limited to, peptides, proteins, hormones, cofactors and nucleic acids. For the purposes of this discussion, such cellular and extracellular molecules are referred to herein as "binding partners" or marker  
30 "substrate".

One necessary embodiment of the invention in order to facilitate such screening is the use of a protein encoded by or corresponding to marker to identify the protein's natural *in vivo* binding partners. There are many ways to accomplish this which are known to one skilled in the art. One example is the use of the marker protein as "bait protein" in a two-hybrid assay or three-hybrid assay (see, *e.g.*, U.S. Patent No. 5,283,317; Zervos *et al*, 1993, *Cell* 72:223-232; Madura *et al*, 1993, *J. Biol. Chem.* 268:12046-12054; Bartel *et al*, 1993, *Biotechniques* 14:920-924; Iwabuchi *et al*, 1993 *Oncogene* 8:1693-1696; Brent WO94/10300) in order to identify other proteins which bind to or interact with the marker (binding partners) and, therefore, are possibly involved in the natural function of the marker. Such marker binding partners are also likely to be involved in the propagation of signals by the marker protein or downstream elements of a marker protein-mediated signaling pathway. Alternatively, such marker protein binding partners may also be found to be inhibitors of the marker protein.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that encodes a marker protein fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming a marker-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be readily detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the protein which interacts with the marker protein.

In a further embodiment, assays may be devised through the use of the invention for the purpose of identifying compounds which modulate (*e.g.*, affect either positively or negatively) interactions between a marker protein and its substrates and/or binding partners. Such compounds can include, but are not limited to, molecules such as antibodies, peptides, hormones, oligonucleotides, nucleic acids, and analogs thereof.

Such compounds may also be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. The preferred assay components for use in this embodiment is an ovarian cancer marker protein identified herein, the known binding partner and/or substrate of same, and the test compound. Test compounds can be  
5 supplied from any source.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the marker protein and its binding partner involves preparing a reaction mixture containing the marker protein and its binding partner under conditions and for a time sufficient to allow the two products to interact  
10 and bind, thus forming a complex. In order to test an agent for inhibitory activity, the reaction mixture is prepared in the presence and absence of the test compound. The test compound can be initially included in the reaction mixture, or can be added at a time subsequent to the addition of the marker protein and its binding partner. Control reaction mixtures are incubated without the test compound or with a placebo. The  
15 formation of any complexes between the marker protein and its binding partner is then detected. The formation of a complex in the control reaction, but less or no such formation in the reaction mixture containing the test compound, indicates that the compound interferes with the interaction of the marker protein and its binding partner. Conversely, the formation of more complex in the presence of compound than in the  
20 control reaction indicates that the compound may enhance interaction of the marker protein and its binding partner.

The assay for compounds that interfere with the interaction of the marker protein with its binding partner may be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring either the marker protein or its binding  
25 partner onto a solid phase and detecting complexes anchored to the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the marker proteins and the binding partners  
30 (*e.g.*, by competition) can be identified by conducting the reaction in the presence of the test substance, *i.e.*, by adding the test substance to the reaction mixture prior to or simultaneously with the marker and its interactive binding partner. Alternatively, test

compounds that disrupt preformed complexes, *e.g.*, compounds with higher binding constants that displace one of the components from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are briefly described below.

5                   In a heterogeneous assay system, either the marker protein or its binding partner is anchored onto a solid surface or matrix, while the other corresponding non-anchored component may be labeled, either directly or indirectly. In practice, microtitre plates are often utilized for this approach. The anchored species can be immobilized by a number of methods, either non-covalent or covalent, that are typically well known to  
10 one who practices the art. Non-covalent attachment can often be accomplished simply by coating the solid surface with a solution of the marker protein or its binding partner and drying. Alternatively, an immobilized antibody specific for the assay component to be anchored can be used for this purpose. Such surfaces can often be prepared in advance and stored.

15                   In related embodiments, a fusion protein can be provided which adds a domain that allows one or both of the assay components to be anchored to a matrix. For example, glutathione-S-transferase/marker fusion proteins or glutathione-S-transferase/binding partner can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, which are then  
20 combined with the test compound or the test compound and either the non-adsorbed marker or its binding partner, and the mixture incubated under conditions conducive to complex formation (*e.g.*, physiological conditions). Following incubation, the beads or microtiter plate wells are washed to remove any unbound assay components, the immobilized complex assessed either directly or indirectly, for example, as described  
25 above. Alternatively, the complexes can be dissociated from the matrix, and the level of marker binding or activity determined using standard techniques.

                  Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either a marker protein or a marker protein binding partner can be immobilized utilizing conjugation of biotin and  
30 streptavidin. Biotinylated marker protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of

streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the protein-immobilized surfaces can be prepared in advance and stored.

In order to conduct the assay, the corresponding partner of the immobilized assay component is exposed to the coated surface with or without the test compound. After the reaction is complete, unreacted assay components are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the non-immobilized component is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed.

Where the non-immobilized component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for the initially non-immobilized species (the antibody, in turn, can be directly labeled or indirectly labeled with, e.g., a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which modulate (inhibit or enhance) complex formation or which disrupt preformed complexes can be detected.

In an alternate embodiment of the invention, a homogeneous assay may be used. This is typically a reaction, analogous to those mentioned above, which is conducted in a liquid phase in the presence or absence of the test compound. The formed complexes are then separated from unreacted components, and the amount of complex formed is determined. As mentioned for heterogeneous assay systems, the order of addition of reactants to the liquid phase can yield information about which test compounds modulate (inhibit or enhance) complex formation and which disrupt preformed complexes.

In such a homogeneous assay, the reaction products may be separated from unreacted assay components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, complexes of molecules may be separated from uncomplexed molecules through a series of centrifugal steps, due to the different sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., *Trends Biochem Sci* 1993 Aug;18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration

chromatography separates molecules based on size, and through the utilization of an appropriate gel filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the complex as compared to the uncomplexed molecules may be exploited to differentially separate the complex from the remaining individual reactants, for example through the use of ion-exchange chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, 1998, *J Mol. Recognit.* 11:141-148; Hage and Tweed, 1997, *J. Chromatogr. B. Biomed. Sci. Appl.*, 699:499-525). Gel electrophoresis may also be employed to separate complexed molecules from unbound species (see, *e.g.*, Ausubel *et al* (eds.), as described in : Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the electrophoretic process, nondenaturing gels in the absence of reducing agent are typically preferred, but conditions appropriate to the particular interactants will be well known to one skilled in the art. Immunoprecipitation is another common technique utilized for the isolation of a protein-protein complex from solution (see, *e.g.*, Ausubel *et al* (eds.), In: Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, all proteins binding to an antibody specific to one of the binding molecules are precipitated from solution by conjugating the antibody to a polymer bead that may be readily collected by centrifugation. The bound assay components are released from the beads (through a specific proteolysis event or other technique well known in the art which will not disturb the protein-protein interaction in the complex), and a second immunoprecipitation step is performed, this time utilizing antibodies specific for the correspondingly different interacting assay component. In this manner, only formed complexes should remain attached to the beads. Variations in complex formation in both the presence and the absence of a test compound can be compared, thus offering information about the ability of the compound to modulate interactions between the marker protein and its binding partner.

Also within the scope of the present invention are methods for direct detection of interactions between the marker protein and its natural binding partner and/or a test compound in a homogeneous or heterogeneous assay system without

further sample manipulation. For example, the technique of fluorescence energy transfer may be utilized (see, *e.g.*, Lakowicz *et al*, U.S. Patent No. 5,631,169; Stavrianopoulos *et al*, U.S. Patent No. 4,868,103). Generally, this technique involves the addition of a fluorophore label on a first 'donor' molecule (*e.g.*, marker or test compound) such that  
5 its emitted fluorescent energy will be absorbed by a fluorescent label on a second, 'acceptor' molecule (*e.g.*, marker or test compound), which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be  
10 differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through  
15 standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter). A test substance which either enhances or hinders participation of one of the species in the preformed complex will result in the generation of a signal variant to that of background. In this way, test substances that modulate interactions between a marker and its binding partner can be identified in controlled assays.

20 In another embodiment, modulators of marker expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of marker mRNA or protein in the cell, is determined. The level of expression of marker mRNA or protein in the presence of the candidate compound is compared to the level of expression of marker mRNA or protein in the absence of the candidate  
25 compound. The candidate compound can then be identified as a modulator of marker expression based on this comparison. For example, when expression of marker mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of marker mRNA or protein expression. Conversely, when expression of marker mRNA  
30 or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of marker mRNA or protein expression. The level of marker mRNA or protein expression

in the cells can be determined by methods described herein for detecting marker mRNA or protein.

In another aspect, the invention pertains to a combination of two or more of the assays described herein. For example, a modulating agent can be identified using  
5 a cell-based or a cell free assay, and the ability of the agent to modulate the activity of a marker protein can be further confirmed *in vivo*, *e.g.*, in a whole animal model for cellular transformation and/or tumorigenesis.

This invention further pertains to novel agents identified by the above-described screening assays. Accordingly, it is within the scope of this invention to  
10 further use an agent identified as described herein in an appropriate animal model. For example, an agent identified as described herein (*e.g.*, an marker modulating agent, an antisense marker nucleic acid molecule, an marker-specific antibody, or an marker-binding partner) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as  
15 described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above-described screening assays for treatments as described herein.

It is understood that appropriate doses of small molecule agents and protein or polypeptide agents depends upon a number of factors within the knowledge of  
20 the ordinarily skilled physician, veterinarian, or researcher. The dose(s) of these agents will vary, for example, depending upon the identity, size, and condition of the subject or sample being treated, further depending upon the route by which the composition is to be administered, if applicable, and the effect which the practitioner desires the agent to have upon the nucleic acid or polypeptide of the invention. Exemplary doses of a small  
25 molecule include milligram or microgram amounts per kilogram of subject or sample weight (*e.g.* about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram). Exemplary doses of a protein or polypeptide include gram, milligram or microgram amounts per kilogram of  
30 subject or sample weight (*e.g.* about 1 microgram per kilogram to about 5 grams per kilogram, about 100 micrograms per kilogram to about 500 milligrams per kilogram, or about 1 milligram per kilogram to about 50 milligrams per kilogram). It is furthermore



understood that appropriate doses of one of these agents depend upon the potency of the agent with respect to the expression or activity to be modulated. Such appropriate doses can be determined using the assays described herein. When one or more of these agents is to be administered to an animal (*e.g.* a human) in order to modulate expression or activity of a polypeptide or nucleic acid of the invention, a physician, veterinarian, or researcher can, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific agent employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediamine-tetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy

syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

15 Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, a polypeptide or antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium, and then incorporating the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

25 Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed.

Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches, and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a  
5 lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the  
10 form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally  
15 known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

20 The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled  
25 release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova  
30 Pharmaceuticals, Inc. Liposomal suspensions (including liposomes having monoclonal antibodies incorporated therein or thereon) can also be used as pharmaceutically

acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit  
5 form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound  
10 and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

For antibodies, the preferred dosage is 0.1 mg/kg to 100 mg/kg of body weight (generally 10 mg/kg to 20 mg/kg). If the antibody is to act in the brain, a dosage of 50 mg/kg to 100 mg/kg is usually appropriate. Generally, partially human antibodies  
15 and fully human antibodies have a longer half-life within the human body than other antibodies. Accordingly, lower dosages and less frequent administration is often possible. Modifications such as lipitation can be used to stabilize antibodies and to enhance uptake and tissue penetration (*e.g.*, into the ovarian epithelium). A method for lipitation of antibodies is described by Cruikshank *et al.* (1997) *J. Acquired Immune*  
20 *Deficiency Syndromes and Human Retrovirology* 14:193.

The invention also provides vaccine compositions for the prevention and/or treatment of ovarian cancer. The invention provides ovarian cancer vaccine compositions in which a protein of a marker of Table 1, or a combination of proteins of the markers of Table 1, are introduced into a subject in order to stimulate an immune  
25 response against the ovarian cancer. The invention also provides ovarian cancer vaccine compositions in which a gene expression construct, which expresses a marker or fragment of a marker identified in Table 1, is introduced into the subject such that a protein or fragment of a protein encoded by a marker of Table 1 is produced by transfected cells in the subject at a higher than normal level and elicits an immune  
30 response.

In one embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the prevention of ovarian cancer. In another embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the treatment of ovarian cancer.

5 By way of example, an ovarian cancer vaccine comprised of the proteins of the markers of Table 1, may be employed for the prevention and/or treatment of ovarian cancer in a subject by administering the vaccine by a variety of routes, *e.g.*, intradermally, subcutaneously, or intramuscularly. In addition, the ovarian cancer vaccine can be administered together with adjuvants and/or immunomodulators to boost  
10 the activity of the vaccine and the subject's response. In one embodiment, devices and/or compositions containing the vaccine, suitable for sustained or intermittent release could be, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body. The ovarian cancer vaccine can be introduced along with immunomodulatory compounds, which can alter the type of immune  
15 response produced in order to produce a response which will be more effective in eliminating the cancer.

In another embodiment, an ovarian cancer vaccine comprised of an expression construct of the markers of Table 1, may be introduced by injection into muscle or by coating onto microprojectiles and using a device designed for the purpose  
20 to fire the projectiles at high speed into the skin. The cells of the subject will then express the protein(s) or fragments of proteins of the markers of Table 1 and induce an immune response. In addition, the ovarian cancer vaccine may be introduced along with expression constructs for immunomodulatory molecules, such as cytokines, which may increase the immune response or modulate the type of immune response produced in  
25 order to produce a response which will be more effective in eliminating the cancer.

The marker nucleic acid molecules of the present invention can also be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470), or by stereotactic injection (see, *e.g.*, Chen *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* 91:3054-3057).  
30 The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively,

where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.* retroviral vectors, the pharmaceutical preparation can include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or  
5 dispenser together with instructions for administration.

## V. Predictive Medicine

The present invention pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical  
10 trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining the level of expression of one or more marker proteins or nucleic acids, in order to determine whether an individual is at risk of developing ovarian cancer. Such assays can be used for prognostic or predictive purposes to thereby  
15 prophylactically treat an individual prior to the onset of the cancer.

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs or other compounds administered either to inhibit ovarian cancer or to treat or prevent any other disorder {*i.e.* in order to understand any ovarian carcinogenic effects that such treatment may have} ) on the expression or activity of a  
20 marker of the invention in clinical trials. These and other agents are described in further detail in the following sections.

### A. Diagnostic Assays

An exemplary method for detecting the presence or absence of a marker  
25 protein or nucleic acid in a biological sample involves obtaining a biological sample (*e.g.* an ovary-associated body fluid) from a test subject and contacting the biological sample with a compound or an agent capable of detecting the polypeptide or nucleic acid (*e.g.*, mRNA, genomic DNA, or cDNA). The detection methods of the invention can thus be used to detect mRNA, protein, cDNA, or genomic DNA, for example, in a  
30 biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of a marker protein include enzyme linked immunosorbent

assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein or fragment thereof. For  
5 example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

A general principle of such diagnostic and prognostic assays involves preparing a sample or reaction mixture that may contain a marker, and a probe, under appropriate conditions and for a time sufficient to allow the marker and probe to interact  
10 and bind, thus forming a complex that can be removed and/or detected in the reaction mixture. These assays can be conducted in a variety of ways.

For example, one method to conduct such an assay would involve anchoring the marker or probe onto a solid phase support, also referred to as a substrate, and detecting target marker/probe complexes anchored on the solid phase at the end of  
15 the reaction. In one embodiment of such a method, a sample from a subject, which is to be assayed for presence and/or concentration of marker, can be anchored onto a carrier or solid phase support. In another embodiment, the reverse situation is possible, in which the probe can be anchored to a solid phase and a sample from a subject can be allowed to react as an unanchored component of the assay.

20 There are many established methods for anchoring assay components to a solid phase. These include, without limitation, marker or probe molecules which are immobilized through conjugation of biotin and streptavidin. Such biotinylated assay components can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and  
25 immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the surfaces with immobilized assay components can be prepared in advance and stored.

Other suitable carriers or solid phase supports for such assays include any material capable of binding the class of molecule to which the marker or probe belongs.  
30 Well-known supports or carriers include, but are not limited to, glass, polystyrene, nylon, polypropylene, nylon, polyethylene, dextran, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

In order to conduct assays with the above mentioned approaches, the non-immobilized component is added to the solid phase upon which the second component is anchored. After the reaction is complete, uncomplexed components may be removed (*e.g.*, by washing) under conditions such that any complexes formed will remain immobilized upon the solid phase. The detection of marker/probe complexes anchored to the solid phase can be accomplished in a number of methods outlined herein.

In a preferred embodiment, the probe, when it is the unanchored assay component, can be labeled for the purpose of detection and readout of the assay, either directly or indirectly, with detectable labels discussed herein and which are well-known to one skilled in the art.

It is also possible to directly detect marker/probe complex formation without further manipulation or labeling of either component (marker or probe), for example by utilizing the technique of fluorescence energy transfer (see, for example, Lakowicz *et al.*, U.S. Patent No. 5,631,169; Stavrianopoulos, *et al.*, U.S. Patent No. 4,868,103). A fluorophore label on the first, 'donor' molecule is selected such that, upon excitation with incident light of appropriate wavelength, its emitted fluorescent energy will be absorbed by a fluorescent label on a second 'acceptor' molecule, which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter).

In another embodiment, determination of the ability of a probe to recognize a marker can be accomplished without labeling either assay component (probe or marker) by utilizing a technology such as real-time Biomolecular Interaction Analysis (BIA) (see, *e.g.*, Sjolander, S. and Urbaniczky, C., 1991, *Anal. Chem.* 63:2338-2345



and Szabo *et al.*, 1995, *Curr. Opin. Struct. Biol.* 5:699-705). As used herein, "BIA" or "surface plasmon resonance" is a technology for studying biospecific interactions in real time, without labeling any of the interactants (*e.g.*, BIAcore). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of surface plasmon resonance (SPR)),  
5 resulting in a detectable signal which can be used as an indication of real-time reactions between biological molecules.

Alternatively, in another embodiment, analogous diagnostic and prognostic assays can be conducted with marker and probe as solutes in a liquid phase.

10 In such an assay, the complexed marker and probe are separated from uncomplexed components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, marker/probe complexes may be separated from uncomplexed assay components through a series of centrifugal steps, due to the different  
15 sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., 1993, *Trends Biochem Sci.* 18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration chromatography separates molecules based on size, and through the utilization of an appropriate gel  
20 filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the marker/probe complex as compared to the uncomplexed components may be exploited to differentiate the complex from uncomplexed components, for example through the utilization of ion-exchange  
25 chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, N.H., 1998, *J. Mol. Recognit.* Winter 11(1-6):141-8; Hage, D.S., and Tweed, S.A. *J Chromatogr B Biomed Sci Appl* 1997 Oct 10;699(1-2):499-525). Gel electrophoresis may also be employed to separate complexed assay components from unbound components (see, *e.g.*, Ausubel *et al.*, ed.,  
30 *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, 1987-1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the

electrophoretic process, non-denaturing gel matrix materials and conditions in the absence of reducing agent are typically preferred. Appropriate conditions to the particular assay and components thereof will be well known to one skilled in the art.

In a particular embodiment, the level of marker mRNA can be  
5 determined both by *in situ* and by *in vitro* formats in a biological sample using methods known in the art. The term "biological sample" is intended to include tissues, cells, biological fluids and isolates thereof, isolated from a subject, as well as tissues, cells and fluids present within a subject. Many expression detection methods use isolated RNA. For *in vitro* methods, any RNA isolation technique that does not select against the  
10 isolation of mRNA can be utilized for the purification of RNA from ovarian cells (see, e.g., Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, New York 1987-1999). Additionally, large numbers of tissue samples can readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski (1989, U.S. Patent No.  
15 4,843,155).

The isolated mRNA can be used in hybridization or amplification assays that include, but are not limited to, Southern or Northern analyses, polymerase chain reaction analyses and probe arrays. One preferred diagnostic method for the detection of mRNA levels involves contacting the isolated mRNA with a nucleic acid molecule  
20 (probe) that can hybridize to the mRNA encoded by the gene being detected. The nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least 7, 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to a mRNA or genomic DNA encoding a marker of the present invention. Other suitable probes for use in the  
25 diagnostic assays of the invention are described herein. Hybridization of an mRNA with the probe indicates that the marker in question is being expressed.

In one format, the mRNA is immobilized on a solid surface and contacted with a probe, for example by running the isolated mRNA on an agarose gel and transferring the mRNA from the gel to a membrane, such as nitrocellulose. In an  
30 alternative format, the probe(s) are immobilized on a solid surface and the mRNA is contacted with the probe(s), for example, in an Affymetrix gene chip array. A skilled

artisan can readily adapt known mRNA detection methods for use in detecting the level of mRNA encoded by the markers of the present invention.

An alternative method for determining the level of mRNA marker in a sample involves the process of nucleic acid amplification, *e.g.*, by rtPCR (the  
5 experimental embodiment set forth in Mullis, 1987, U.S. Patent No. 4,683,202), ligase chain reaction (Barany, 1991, *Proc. Natl. Acad. Sci. USA*, 88:189-193), self sustained sequence replication (Guatelli *et al.*, 1990, *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi *et al.*, 1988, *Bio/Technology* 6:1197), rolling  
10 circle replication (Lizardi *et al.*, U.S. Patent No. 5,854,033) or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers. As used herein, amplification primers are defined as being  
15 a pair of nucleic acid molecules that can anneal to 5' or 3' regions of a gene (plus and minus strands, respectively, or vice-versa) and contain a short region in between. In general, amplification primers are from about 10 to 30 nucleotides in length and flank a region from about 50 to 200 nucleotides in length. Under appropriate conditions and with appropriate reagents, such primers permit the amplification of a nucleic acid  
20 molecule comprising the nucleotide sequence flanked by the primers.

For *in situ* methods, mRNA does not need to be isolated from the ovarian cells prior to detection. In such methods, a cell or tissue sample is prepared/processed using known histological methods. The sample is then immobilized on a support, typically a glass slide, and then contacted with a probe that can hybridize to mRNA that  
25 encodes the marker.

As an alternative to making determinations based on the absolute expression level of the marker, determinations may be based on the normalized expression level of the marker. Expression levels are normalized by correcting the absolute expression level of a marker by comparing its expression to the expression of a  
30 gene that is not a marker, *e.g.*, a housekeeping gene that is constitutively expressed. Suitable genes for normalization include housekeeping genes such as the actin gene, or epithelial cell-specific genes. This normalization allows the comparison of the

expression level in one sample, *e.g.*, a patient sample, to another sample, *e.g.*, a non-ovarian cancer sample, or between samples from different sources.

Alternatively, the expression level can be provided as a relative expression level. To determine a relative expression level of a marker, the level of  
5 expression of the marker is determined for 10 or more samples of normal versus cancer cell isolates, preferably 50 or more samples, prior to the determination of the expression level for the sample in question. The mean expression level of each of the genes assayed in the larger number of samples is determined and this is used as a baseline expression level for the marker. The expression level of the marker determined for the  
10 test sample (absolute level of expression) is then divided by the mean expression value obtained for that marker. This provides a relative expression level.

Preferably, the samples used in the baseline determination will be from ovarian cancer or from non-ovarian cancer cells of ovarian tissue. The choice of the cell source is dependent on the use of the relative expression level. Using expression found  
15 in normal tissues as a mean expression score aids in validating whether the marker assayed is ovarian specific (versus normal cells). In addition, as more data is accumulated, the mean expression value can be revised, providing improved relative expression values based on accumulated data. Expression data from ovarian cells provides a means for grading the severity of the ovarian cancer state.

20 In another embodiment of the present invention, a marker protein is detected. A preferred agent for detecting marker protein of the invention is an antibody capable of binding to such a protein or a fragment thereof, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment or derivatives thereof (*e.g.*, Fab or F(ab')<sub>2</sub>) can be used.  
25 The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody  
30 and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin.

Proteins from ovarian cells can be isolated using techniques that are well known to those of skill in the art. The protein isolation methods employed can, for example, be such as those described in Harlow and Lane (Harlow and Lane, 1988, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

A variety of formats can be employed to determine whether a sample contains a protein that binds to a given antibody. Examples of such formats include, but are not limited to, enzyme immunoassay (EIA), radioimmunoassay (RIA), Western blot analysis and enzyme linked immunoabsorbant assay (ELISA). A skilled artisan can readily adapt known protein/antibody detection methods for use in determining whether ovarian cells express a marker of the present invention.

In one format, antibodies, or antibody fragments or derivatives, can be used in methods such as Western blots or immunofluorescence techniques to detect the expressed proteins. In such uses, it is generally preferable to immobilize either the antibody or proteins on a solid support. Suitable solid phase supports or carriers include any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

One skilled in the art will know many other suitable carriers for binding antibody or antigen, and will be able to adapt such support for use with the present invention. For example, protein isolated from ovarian cells can be run on a polyacrylamide gel electrophoresis and immobilized onto a solid phase support such as nitrocellulose. The support can then be washed with suitable buffers followed by treatment with the detectably labeled antibody. The solid phase support can then be washed with the buffer a second time to remove unbound antibody. The amount of bound label on the solid support can then be detected by conventional means.

The invention also encompasses kits for detecting the presence of a marker protein or nucleic acid in a biological sample (e.g. an ovary-associated body fluid such as a urine sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing ovarian cancer. For example, the kit can comprise a labeled compound or agent capable of detecting a marker protein or nucleic acid in a biological sample and means for determining the amount of the protein or

mRNA in the sample (*e.g.*, an antibody which binds the protein or a fragment thereof, or an oligonucleotide probe which binds to DNA or mRNA encoding the protein). Kits can also include instructions for interpreting the results obtained using the kit.

For antibody-based kits, the kit can comprise, for example: (1) a first  
5 antibody (*e.g.*, attached to a solid support) which binds to a marker protein; and, optionally, (2) a second, different antibody which binds to either the protein or the first antibody and is conjugated to a detectable label.

For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, *e.g.*, a detectably labeled oligonucleotide, which hybridizes to a nucleic  
10 acid sequence encoding a marker protein or (2) a pair of primers useful for amplifying a marker nucleic acid molecule. The kit can also comprise, *e.g.*, a buffering agent, a preservative, or a protein stabilizing agent. The kit can further comprise components necessary for detecting the detectable label (*e.g.*, an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and  
15 compared to the test sample. Each component of the kit can be enclosed within an individual container and all of the various containers can be within a single package, along with instructions for interpreting the results of the assays performed using the kit.

#### B. Pharmacogenomics

20 Agents or modulators which have a stimulatory or inhibitory effect on expression of a marker of the invention can be administered to individuals to treat (prophylactically or therapeutically) ovarian cancer in the patient. In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of  
25 the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such  
30 pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the level of expression of a marker of the invention in an

individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, a PM will show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the level of expression of a marker of the invention in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the  
5 identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a modulator of expression of a marker of the invention.

10 C. Monitoring Clinical Trials

Monitoring the influence of agents (*e.g.*, drug compounds) on the level of expression of a marker of the invention can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent to affect marker expression can be monitored in clinical trials of subjects receiving treatment for ovarian  
15 cancer. In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of one  
20 or more selected markers of the invention in the pre-administration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression of the marker(s) in the post-administration samples; (v) comparing the level of expression of the marker(s) in the pre-administration sample with the level of expression of the marker(s) in the post-administration sample or samples; and (vi)  
25 altering the administration of the agent to the subject accordingly. For example, increased administration of the agent can be desirable to increase expression of the marker(s) to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent can be desirable to decrease expression of the marker(s) to lower levels than detected, *i.e.*, to decrease the  
30 effectiveness of the agent.



#### D. Electronic Apparatus Readable Media and Arrays

Electronic apparatus readable media comprising a marker of the present invention is also provided. As used herein, "electronic apparatus readable media" refers to any suitable medium for storing, holding or containing data or information that can be  
5 read and accessed directly by an electronic apparatus. Such media can include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as compact disc; electronic storage media such as RAM, ROM, EPROM, EEPROM and the like; general hard disks and hybrids of these categories such as magnetic/optical storage media. The medium is adapted or  
10 configured for having recorded thereon a marker of the present invention.

As used herein, the term "electronic apparatus" is intended to include any suitable computing or processing apparatus or other device configured or adapted for storing data or information. Examples of electronic apparatus suitable for use with the present invention include stand-alone computing apparatus; networks, including a local  
15 area network (LAN), a wide area network (WAN) Internet, Intranet, and Extranet; electronic appliances such as a personal digital assistants (PDAs), cellular phone, pager and the like; and local and distributed processing systems.

As used herein, "recorded" refers to a process for storing or encoding information on the electronic apparatus readable medium. Those skilled in the art can  
20 readily adopt any of the presently known methods for recording information on known media to generate manufactures comprising the markers of the present invention.

A variety of software programs and formats can be used to store the marker information of the present invention on the electronic apparatus readable medium. For example, the marker nucleic acid sequence can be represented in a word  
25 processing text file, formatted in commercially-available software such as WordPerfect and MicroSoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like, as well as in other forms. Any number of data processor structuring formats (e.g., text file or database) may be employed in order to obtain or create a medium having recorded thereon the the markers  
30 of the present invention.

By providing the markers of the invention in readable form, one can routinely access the marker sequence information for a variety of purposes. For example, one skilled in the art can use the nucleotide or amino acid sequences of the present invention in readable form to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of the sequences of the invention which match a particular target sequence or target motif.

The present invention therefore provides a medium for holding instructions for performing a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, wherein the method comprises the steps of determining the presence or absence of a marker and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer and/or recommending a particular treatment for ovarian cancer or pre-ovarian cancer condition.

The present invention further provides in an electronic system and/or in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker wherein the method comprises the steps of determining the presence or absence of the marker, and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer, and/or recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition. The method may further comprise the step of receiving phenotypic information associated with the subject and/or acquiring from a network phenotypic information associated with the subject.

The present invention also provides in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker; said method comprising the steps of receiving information associated with the marker receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has a ovarian cancer or a pre-disposition to ovarian cancer. The method may further comprise the step of

recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The present invention also provides a business method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, said method comprising the steps of receiving information associated with the marker, receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer. The method may further comprise the step of recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The invention also includes an array comprising a marker of the present invention. The array can be used to assay expression of one or more genes in the array. In one embodiment, the array can be used to assay gene expression in a tissue to ascertain tissue specificity of genes in the array. In this manner, up to about 7600 genes can be simultaneously assayed for expression. This allows a profile to be developed showing a battery of genes specifically expressed in one or more tissues.

In addition to such qualitative determination, the invention allows the quantitation of gene expression. Thus, not only tissue specificity, but also the level of expression of a battery of genes in the tissue is ascertainable. Thus, genes can be grouped on the basis of their tissue expression *per se* and level of expression in that tissue. This is useful, for example, in ascertaining the relationship of gene expression between or among tissues. Thus, one tissue can be perturbed and the effect on gene expression in a second tissue can be determined. In this context, the effect of one cell type on another cell type in response to a biological stimulus can be determined. Such a determination is useful, for example, to know the effect of cell-cell interaction at the level of gene expression. If an agent is administered therapeutically to treat one cell type but has an undesirable effect on another cell type, the invention provides an assay to determine the molecular basis of the undesirable effect and thus provides the opportunity to co-administer a counteracting agent or otherwise treat the undesired effect. Similarly, even within a single cell type, undesirable biological effects can be

determined at the molecular level. Thus, the effects of an agent on expression of other than the target gene can be ascertained and counteracted.

In another embodiment, the array can be used to monitor the time course of expression of one or more genes in the array. This can occur in various biological contexts, as disclosed herein, for example development of ovarian cancer, progression of ovarian cancer, and processes, such as cellular transformation associated with ovarian cancer.

The array is also useful for ascertaining the effect of the expression of a gene on the expression of other genes in the same cell or in different cells. This provides, for example, for a selection of alternate molecular targets for therapeutic intervention if the ultimate or downstream target cannot be regulated.

The array is also useful for ascertaining differential expression patterns of one or more genes in normal and abnormal cells. This provides a battery of genes that could serve as a molecular target for diagnosis or therapeutic intervention.

15

#### E. Surrogate Markers

The markers of the invention may serve as surrogate markers for one or more disorders or disease states or for conditions leading up to disease states, and in particular, ovarian cancer. As used herein, a "surrogate marker" is an objective biochemical marker which correlates with the absence or presence of a disease or disorder, or with the progression of a disease or disorder (*e.g.*, with the presence or absence of a tumor). The presence or quantity of such markers is independent of the disease. Therefore, these markers may serve to indicate whether a particular course of treatment is effective in lessening a disease state or disorder. Surrogate markers are of particular use when the presence or extent of a disease state or disorder is difficult to assess through standard methodologies (*e.g.*, early stage tumors), or when an assessment of disease progression is desired before a potentially dangerous clinical endpoint is reached (*e.g.*, an assessment of cardiovascular disease may be made using cholesterol levels as a surrogate marker, and an analysis of HIV infection may be made using HIV RNA levels as a surrogate marker, well in advance of the undesirable clinical outcomes of myocardial infarction or fully-developed AIDS). Examples of the use of surrogate

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markers in the art include: Koomen *et al.* (2000) *J. Mass. Spectrom.* 35: 258-264; and James (1994) *AIDS Treatment News Archive* 209.

The markers of the invention are also useful as pharmacodynamic markers. As used herein, a "pharmacodynamic marker" is an objective biochemical marker which correlates specifically with drug effects. The presence or quantity of a pharmacodynamic marker is not related to the disease state or disorder for which the drug is being administered; therefore, the presence or quantity of the marker is indicative of the presence or activity of the drug in a subject. For example, a pharmacodynamic marker may be indicative of the concentration of the drug in a biological tissue, in that the marker is either expressed or transcribed or not expressed or transcribed in that tissue in relationship to the level of the drug. In this fashion, the distribution or uptake of the drug may be monitored by the pharmacodynamic marker. Similarly, the presence or quantity of the pharmacodynamic marker may be related to the presence or quantity of the metabolic product of a drug, such that the presence or quantity of the marker is indicative of the relative breakdown rate of the drug *in vivo*. Pharmacodynamic markers are of particular use in increasing the sensitivity of detection of drug effects, particularly when the drug is administered in low doses. Since even a small amount of a drug may be sufficient to activate multiple rounds of marker transcription or expression, the amplified marker may be in a quantity which is more readily detectable than the drug itself. Also, the marker may be more easily detected due to the nature of the marker itself; for example, using the methods described herein, antibodies may be employed in an immune-based detection system for a protein marker, or marker-specific radiolabeled probes may be used to detect a mRNA marker. Furthermore, the use of a pharmacodynamic marker may offer mechanism-based prediction of risk due to drug treatment beyond the range of possible direct observations. Examples of the use of pharmacodynamic markers in the art include: Matsuda *et al.* US 6,033,862; Hattis *et al.* (1991) *Env. Health Perspect.* 90: 229-238; Schentag (1999) *Am. J. Health-Syst. Pharm.* 56 Suppl. 3: S21-S24; and Nicolau (1999) *Am. J. Health-Syst. Pharm.* 56 Suppl. 3: S16-S20.

## VI. Experimental Protocol for all OV markers and M352 - M360

### A. Identification of markers

The markers of the present invention were identified by transcriptional  
5 profiling using mRNA from 9 normal ovarian epithelia, 11 stage I/II ovarian cancer  
tumors and 25 stage III/IV tumors. Clones having expression at least two-fold higher in  
ovarian tumors as compared to their expression in non-ovarian tumor tissues in at least 4  
tumor samples were selected to have their protein-encoding transcript sequences  
determined.

10

### B. Identification of Markers and Assembly of Their Sequences

Clones which displayed an increase in expression in ovarian tumor  
samples over the corresponding average expression of non-tumor samples were used for  
further study. Briefly, BLAST analysis, against both public and proprietary sequence  
15 databases, of EST sequences known to be associated with each clone was performed,  
either directly or in the context of automatically, high-stringency assembled contiguous  
sequences. An identification of protein sequence corresponding to the clone was  
accomplished by obtaining one of the following:

- a) a direct match between the protein sequence and at least one EST  
20 sequence in one of its 6 possible translations;
- b) a direct match between the nucleotide sequence for the mRNA  
corresponding to the protein sequence and at least one EST sequence;
- c) a match between the protein sequence and a contiguous assembly  
(contig) of the EST sequences with other available EST sequences in the databases in  
25 one of its 6 possible translations; or
- d) a match between the nucleotide sequence for the mRNA  
corresponding to the protein sequence and a contiguous assembly of the EST sequences  
with other available EST sequences in the databases in one of its 6 possible translations.

C. Identification of Markers Having Newly-Identified Nucleotide and Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences.

- 5 These sequences were found to be novel based on one of the following criteria:
- a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;
  - b) based on nucleotide evidence, variants of the protein sequence were
  - 10 additionally constructed that are not found as such in the public domain; or
  - c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

- 15 VII. Experimental Protocol for M68, M103, M138, M185, M312, M327-M328, M400, M430-M480, M559, M571-M573, M575-M576, M578-M583, M585-594, and M604-M617

A. Identification of Markers and Assembly of Their Sequences

- 20 The markers of the present invention were identified by transcription profiling using mRNA from 67 ovarian tumors of various histotypes and stage and 96 non-ovarian tumor tissues including normal ovarian epithelium, benign conditions, other normal tissues, and other abnormal tissues. Clones having expression at least three-fold higher in at least 10% of ovarian tumors, as compared to their expression in non-ovarian
- 25 tumor tissue, were designated as ovarian cancer specific markers. These cDNA clones were selected to have their protein-encoding transcript sequences determined. Briefly, BLAST analysis, against both public and proprietary sequence databases, of EST sequences known to be associated with each clone was performed, either directly or in the context of automatically, high-stringency assembled contiguous sequences. An
- 30 identification of protein sequence corresponding to the clone was accomplished by obtaining one of the following:
- a) a direct match between the protein sequence and at least one EST sequence in one of its 6 possible translations;

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- b) a direct match between the nucleotide sequence for the mRNA corresponding to the protein sequence and at least one EST sequence;
- c) a match between the protein sequence and a contiguous assembly (contig) of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations; or
- d) a match between the nucleotide sequence for the mRNA corresponding to the protein sequence and a contiguous assembly of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations.

10                    B. Identification of Markers Having Newly-Identified Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences. These sequences were found to be novel based on one of the following criteria:

- a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;
- b) based on nucleotide evidence, variants of the protein sequence were additionally constructed that are not found as such in the public domain; or
- c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

VIII. Gene Expression Analysis

Total RNA from normal human tissue was obtained from commercial sources. The integrity of the RNA was verified by agarose gel electrophoresis and ethidium bromide staining. Cell lines were purchased from ATCC and grown under the conditions recommended by ATCC. Total RNA from a number of various cell lines was prepared using commercial kits (Qiagen). First strand cDNA was prepared using oligo-dT primer and standard conditions. Each RNA preparation was treated with DNase I (Ambion) at 37°C for 1 hour.

30                    Novel gene expression was measured by TaqMan<sup>®</sup> quantitative PCR (Perkin Elmer Applied Biosystems) in cDNA prepared from the following normal human tissues: heart, kidney, skeletal muscle, pancreas, skin, dorsal root ganglion,



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breast, ovary, prostate, salivary glands, lung, colon, liver and lymph node. Figure 1 graphically represents the results of the TaqMan® expression study. The columns labelled A to V depict the expression level observed for OV88 in the following tissues:

- Column A: Heart, normal tissue
- 5 Column B: Heart, CHF tissue
- Column C: Kidney, normal tissue
- Column D: Skeletal muscle, normal tissue
- Column E: Pancreas, normal tissue
- Column F: Skin, normal tissue
- 10 Column G: Dorsal root, normal tissue
- Column H: Breast, normal tissue
- Column I: Breast, tumor tissue
- Column J: Ovary, normal tissue
- Column K: Ovary, tumor tissue
- 15 Column L: Prostate, normal tissue
- Column M: Prostate, tumor tissue
- Column N: Salivary glands, normal tissue
- Column O: Lung, normal tissue
- Column P: Lung, tumor tissue
- 20 Column Q: Lung, COPD tissue
- Column R: Colon, IBD tissue
- Column S: Liver, normal tissue
- Column T: Liver fibrosis
- Column U: Lymph node, normal tissue
- 25 Column V: Positive control

#### IX. Summary of the Data Provided in the Tables

Tables 1-3 list the markers of the present invention. In the Tables the markers are identified with a name ("Marker"), the name the gene is commonly known  
 30 by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded

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by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein coding sequence within the cDNA sequence ("CDS").

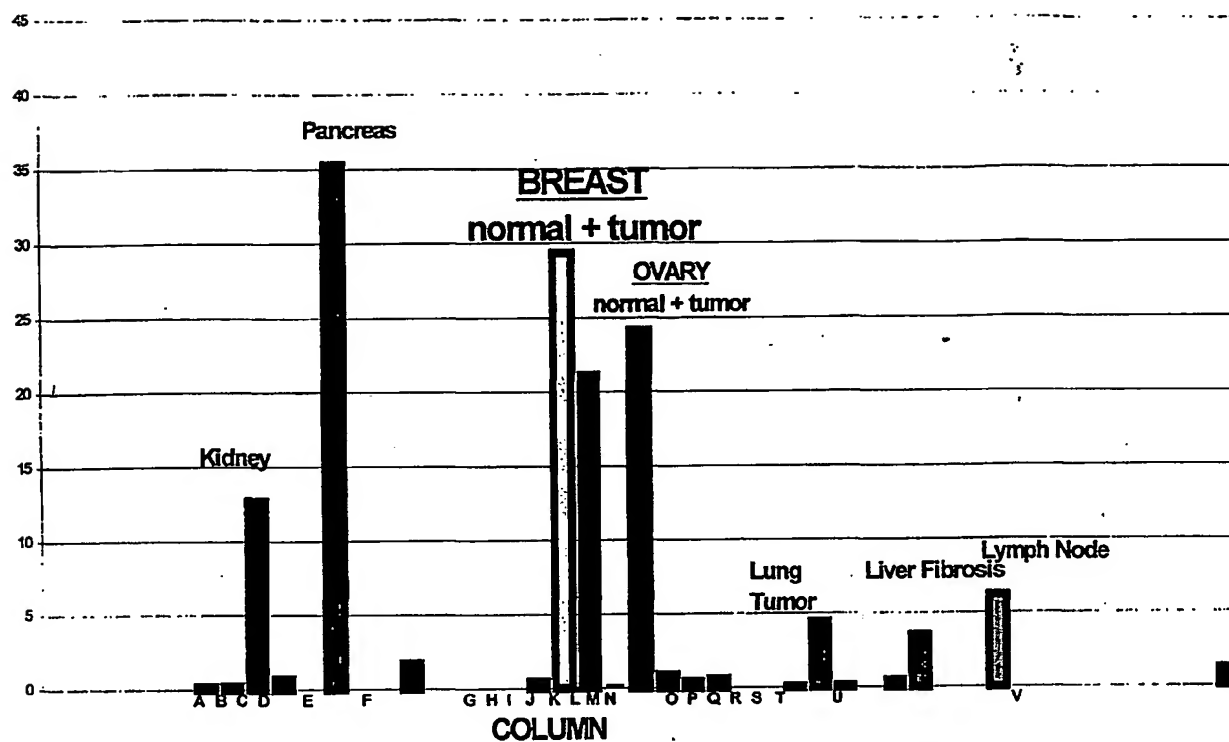
Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and  
5 comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

#### Other Embodiments

10 Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims:

What is claimed:

1. A method of assessing whether a patient is afflicted with ovarian cancer, the method comprising comparing:
  - 5 a) the level of expression of a marker in a patient sample, wherein the marker is selected from Table 1, and
  - b) the normal level of expression of the marker in a control non-ovarian cancer sample,wherein a significant increase in the level of expression of the marker in  
10 the patient sample and the normal level is an indication that the patient is afflicted with ovarian cancer.

Figure 1

## SEQUENCE LISTING

<110> Millennium Pharmaceuticals, Inc. et al.

<120> Nucleic Acid Molecules and Proteins For The Identification, Assessment, Prevention, and Therapy of Ovarian Cancer

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<151> 2001-03-14

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<400> 2

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Phe	Lys	Leu	Asn	Asn	Lys	Ser	Glu	Lys	Asp	Lys	Lys	Glu	Lys	Lys	Pro	20	25	30	
Thr	Val	Ser	Val	Phe	Ser	Met	Phe	Arg	Tyr	Ser	Asn	Trp	Leu	Asp	Lys	35	40	45	
Leu	Tyr	Met	Val	Val	Gly	Thr	Leu	Ala	Ala	Ile	Ile	His	Gly	Ala	Gly	50	55	60	
Leu	Pro	Leu	Met	Met	Leu	Val	Phe	Gly	Glu	Met	Thr	Asp	Ile	Phe	Ala	65	70	75	80
Asn	Ala	Gly	Asn	Leu	Glu	Asp	Leu	Met	Ser	Asn	Ile	Thr	Asn	Arg	Ser	85	90	95	
Asp	Ile	Asn	Asp	Thr	Gly	Phe	Phe	Met	Asn	Leu	Glu	Glu	Asp	Met	Thr	100	105	110	
Arg	Tyr	Ala	Tyr	Tyr	Tyr	Ser	Gly	Ile	Gly	Ala	Gly	Val	Leu	Val	Ala	115	120	125	
Ala	Tyr	Ile	Gln	Val	Ser	Phe	Trp	Cys	Leu	Ala	Ala	Gly	Arg	Gln	Ile	130	135	140	
His	Lys	Ile	Arg	Lys	Gln	Phe	Phe	His	Ala	Ile	Met	Arg	Gln	Glu	Ile	145	150	155	160
Gly	Trp	Phe	Asp	Val	His	Asp	Val	Gly	Glu	Leu	Asn	Thr	Arg	Leu	Thr	165	170	175	
Asp	Asp	Val	Ser	Lys	Ile	Asn	Glu	Gly	Ile	Gly	Asp	Lys	Ile	Gly	Met	180	185	190	
Phe	Phe	Gln	Ser	Met	Ala	Thr	Phe	Phe	Thr	Gly	Phe	Ile	Val	Gly	Phe	195	200	205	
Thr	Arg	Gly	Trp	Lys	Leu	Thr	Leu	Val	Ile	Leu	Ala	Ile	Ser	Pro	Val	210	215	220	
Leu	Gly	Leu	Ser	Ala	Ala	Val	Trp	Ala	Lys	Ile	Leu	Ser	Ser	Phe	Thr	225	230	235	240
Asp	Lys	Glu	Leu	Leu	Ala	Tyr	Ala	Lys	Ala	Gly	Ala	Val	Ala	Glu	Glu	245	250	255	
Val	Leu	Ala	Ala	Ile	Arg	Thr	Val	Ile	Ala	Phe	Gly	Gly	Gln	Lys	Lys	260	265	270	
Glu	Leu	Glu	Arg	Tyr	Asn	Lys	Asn	Leu	Glu	Glu	Ala	Lys	Arg	Ile	Gly	275	280	285	
Ile	Lys	Lys	Ala	Ile	Thr	Ala	Asn	Ile	Ser	Ile	Gly	Ala	Ala	Phe	Leu	290	295	300	
Leu	Ile	Tyr	Ala	Ser	Tyr	Ala	Leu	Ala	Phe	Trp	Tyr	Gly	Thr	Thr	Leu	305	310	315	320
Val	Leu	Ser	Gly	Glu	Tyr	Ser	Ile	Gly	Gln	Val	Leu	Thr	Val	Phe	Ser	325	330	335	
Val	Leu	Ile	Gly	Ala	Phe	Ser	Val	Gly	Gln	Ala	Ser	Pro	Ser	Ile	Glu	340	345	350	
Ala	Phe	Ala	Asn	Ala	Arg	Gly	Ala	Ala	Tyr	Glu	Ile	Phe	Lys	Ile	Ile	355	360	365	
Asp	Asn	Lys	Pro	Ser	Ile	Asp	Ser	Tyr	Ser	Lys	Ser	Gly	His	Lys	Pro	370	375	380	

Asp Asn Ile Lys Gly Asn Leu Glu Phe Arg Asn Val His Phe Ser Tyr  
 385 390 395 400  
 Pro Ser Arg Lys Glu Val Lys Ile Leu Lys Gly Leu Asn Leu Lys Val  
 405 410 415  
 Gln Ser Gly Gln Thr Val Ala Leu Val Gly Asn Ser Gly Cys Gly Lys  
 420 425 430  
 Ser Thr Thr Val Gln Leu Met Gln Arg Leu Tyr Asp Pro Thr Glu Gly  
 435 440 445  
 Met Val Ser Val Asp Gly Gln Asp Ile Arg Thr Ile Asn Val Arg Phe  
 450 455 460  
 Leu Arg Glu Ile Ile Gly Val Val Ser Gln Glu Pro Val Leu Phe Ala  
 465 470 475 480  
 Thr Thr Ile Ala Glu Asn Ile Arg Tyr Gly Arg Glu Asn Val Thr Met  
 485 490 495  
 Asp Glu Ile Glu Lys Ala Val Lys Glu Ala Asn Ala Tyr Asp Phe Ile  
 500 505 510  
 Met Lys Leu Pro His Lys Phe Asp Thr Leu Val Gly Glu Arg Gly Ala  
 515 520 525  
 Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg Ala Leu  
 530 535 540  
 Val Arg Asn Pro Lys Ile Leu Leu Leu Asp Glu Ala Thr Ser Ala Leu  
 545 550 555 560  
 Asp Thr Glu Ser Glu Ala Val Val Gln Val Ala Leu Asp Lys Ala Arg  
 565 570 575  
 Lys Gly Arg Thr Thr Ile Val Ile Ala His Arg Leu Ser Thr Val Arg  
 580 585 590  
 Asn Ala Asp Val Ile Ala Gly Phe Asp Asp Gly Val Ile Val Glu Lys  
 595 600 605  
 Gly Asn His Asp Glu Leu Met Lys Glu Lys Gly Ile Tyr Phe Lys Leu  
 610 615 620  
 Val Thr Met Gln Thr Ala Gly Asn Glu Val Glu Leu Glu Asn Ala Ala  
 625 630 635 640  
 Asp Glu Ser Lys Ser Glu Ile Asp Ala Leu Glu Met Ser Ser Asn Asp  
 645 650 655  
 Ser Arg Ser Ser Leu Ile Arg Lys Arg Ser Thr Arg Arg Ser Val Arg  
 660 665 670  
 Gly Ser Gln Ala Gln Asp Arg Lys Leu Ser Thr Lys Glu Ala Leu Asp  
 675 680 685  
 Glu Ser Ile Pro Pro Val Ser Phe Trp Arg Ile Met Lys Leu Asn Leu  
 690 695 700  
 Thr Glu Trp Pro Tyr Phe Val Val Gly Val Phe Cys Ala Ile Ile Asn  
 705 710 715 720  
 Gly Gly Leu Gln Pro Ala Phe Ala Ile Ile Phe Ser Lys Ile Ile Gly  
 725 730 735  
 Val Phe Thr Arg Ile Asp Asp Pro Glu Thr Lys Arg Gln Asn Ser Asn  
 740 745 750  
 Leu Phe Ser Leu Leu Phe Leu Ala Leu Gly Ile Ile Ser Phe Ile Thr  
 755 760 765  
 Phe Phe Leu Gln Gly Phe Thr Phe Gly Lys Ala Gly Glu Ile Leu Thr  
 770 775 780  
 Lys Arg Leu Arg Tyr Met Val Phe Arg Ser Met Leu Arg Gln Asp Val  
 785 790 795 800  
 Ser Trp Phe Asp Asp Pro Lys Asn Thr Thr Gly Ala Leu Thr Thr Arg  
 805 810 815  
 Leu Ala Asn Asp Ala Ala Gln Val Lys Gly Ala Ile Gly Ser Arg Leu  
 820 825 830  
 Ala Val Ile Thr Gln Asn Ile Ala Asn Leu Gly Thr Gly Ile Ile Ile  
 835 840 845



Ser Phe Ile Tyr Gly Trp Gln Leu Thr Leu Leu Leu Leu Ala Ile Val  
 850 855 860  
 Pro Ile Ile Ala Ile Ala Gly Val Val Glu Met Lys Met Leu Ser Gly  
 865 870 875 880  
 Gln Ala Leu Lys Asp Lys Lys Glu Leu Glu Gly Ala Gly Lys Ile Ala  
 885 890 895  
 Thr Glu Ala Ile Glu Asn Phe Arg Thr Val Val Ser Leu Thr Gln Glu  
 900 905 910  
 Gln Lys Phe Glu His Met Tyr Ala Gln Ser Leu Gln Val Pro Tyr Arg  
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 Asn Ser Leu Arg Lys Ala His Ile Phe Gly Ile Thr Phe Ser Phe Thr  
 930 935 940  
 Gln Ala Met Met Tyr Phe Ser Tyr Ala Gly Cys Phe Arg Phe Gly Ala  
 945 950 955 960  
 Tyr Leu Val Ala His Lys Leu Met Ser Phe Glu Asp Val Leu Leu Val  
 965 970 975  
 Phe Ser Ala Val Val Phe Gly Ala Met Ala Val Gly Gln Val Ser Ser  
 980 985 990  
 Phe Ala Pro Asp Tyr Ala Lys Ala Lys Ile Ser Ala Ala His Ile Ile  
 995 1000 1005  
 Met Ile Ile Glu Lys Thr Pro Leu Ile Asp Ser Tyr Ser Thr Glu Gly  
 1010 1015 1020  
 Leu Met Pro Asn Thr Leu Glu Gly Asn Val Thr Phe Gly Glu Val Val  
 1025 1030 1035 1040  
 Phe Asn Tyr Pro Thr Arg Pro Asp Ile Pro Val Leu Gln Gly Leu Ser  
 1045 1050 1055  
 Leu Glu Val Lys Lys Gly Gln Thr Leu Ala Leu Val Gly Ser Ser Gly  
 1060 1065 1070  
 Cys Gly Lys Ser Thr Val Val Gln Leu Leu Glu Arg Phe Tyr Asp Pro  
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 1090 1095 1100  
 Val Gln Trp Leu Arg Ala His Leu Gly Ile Val Ser Gln Glu Pro Ile  
 1105 1110 1115 1120  
 Leu Phe Asp Cys Ser Ile Ala Glu Asn Ile Ala Tyr Gly Asp Asn Ser  
 1125 1130 1135  
 Arg Val Val Ser Gln Glu Glu Ile Val Arg Ala Ala Lys Glu Ala Asn  
 1140 1145 1150  
 Ile His Ala Phe Ile Glu Ser Leu Pro Asn Lys Tyr Ser Thr Lys Val  
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 Gly Asp Lys Gly Thr Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala  
 1170 1175 1180  
 Ile Ala Arg Ala Leu Val Arg Gln Pro His Ile Leu Leu Leu Asp Glu  
 1185 1190 1195 1200  
 Ala Thr Ser Ala Leu Asp Thr Glu Ser Glu Lys Val Val Gln Glu Ala  
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 Leu Asp Lys Ala Arg Glu Gly Arg Thr Cys Ile Val Ile Ala His Arg  
 1220 1225 1230  
 Leu Ser Thr Ile Gln Asn Ala Asp Leu Ile Val Val Phe Gln Asn Gly  
 1235 1240 1245  
 Arg Val Lys Glu His Gly Thr His Gln Gln Leu Leu Ala Gln Lys Gly  
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 Ile Tyr Phe Ser Met Val Ser Val Gln Ala Gly Thr Lys Arg Gln  
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&lt;210&gt; 3

&lt;211&gt; 3859

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 3

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gacgttgagg tggatgggtt ctctgagctt cggtgggatg accagcagaa agtcaagaag 420
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&lt;210&gt; 4

&lt;211&gt; 1014

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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Met Ala Glu Ser Ser Asp Lys Leu Tyr Arg Val Glu Tyr Ala Lys Ser
1          5          10          15
Gly Arg Ala Ser Cys Lys Lys Cys Ser Glu Ser Ile Pro Lys Asp Ser
20        25        30
Leu Arg Met Ala Ile Met Val Gln Ser Pro Met Phe Asp Gly Lys Val
35        40        45
Pro His Trp Tyr His Phe Ser Cys Phe Trp Lys Val Gly His Ser Ile
50        55        60
Arg His Pro Asp Val Glu Val Asp Gly Phe Ser Glu Leu Arg Trp Asp
65        70        75        80
Asp Gln Gln Lys Val Lys Lys Thr Ala Glu Ala Gly Gly Val Thr Gly
85        90        95
Lys Gly Gln Asp Gly Ile Gly Ser Lys Ala Glu Lys Thr Leu Gly Asp
100       105       110
Phe Ala Ala Glu Tyr Ala Lys Ser Asn Arg Ser Thr Cys Lys Gly Cys
115       120       125
Met Glu Lys Ile Glu Lys Gly Gln Val Arg Leu Ser Lys Lys Met Val
130       135       140
Asp Pro Glu Lys Pro Gln Leu Gly Met Ile Asp Arg Trp Tyr His Pro
145       150       155       160
Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr
165       170       175
Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys
180       185       190
Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg
195       200       205
Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys Lys Ser
210       215       220
Lys Lys Glu Lys Asp Lys Asp Ser Lys Leu Glu Lys Ala Leu Lys Ala
225       230       235       240
Gln Asn Asp Leu Ile Trp Asn Ile Lys Asp Glu Leu Lys Lys Val Cys
245       250       255
Ser Thr Asn Asp Leu Lys Glu Leu Leu Ile Phe Asn Lys Gln Gln Val
260       265       270
Pro Ser Gly Glu Ser Ala Ile Leu Asp Arg Val Ala Asp Gly Met Val
275       280       285
Phe Gly Ala Leu Leu Pro Cys Glu Glu Cys Ser Gly Gln Leu Val Phe
290       295       300
Lys Ser Asp Ala Tyr Tyr Cys Thr Gly Asp Val Thr Ala Trp Thr Lys
305       310       315       320

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Cys Met Val Lys Thr Gln Thr Pro Asn Arg Lys Glu Trp Val Thr Pro	325	330	335
Lys Glu Phe Arg Glu Ile Ser Tyr Leu Lys Lys Leu Lys Val Lys Lys	340	345	350
Gln Asp Arg Ile Phe Pro Pro Glu Thr Ser Ala Ser Val Ala Ala Thr	355	360	365
Pro Pro Pro Ser Thr Ala Ser Ala Pro Ala Ala Val Asn Ser Ser Ala	370	375	380
Ser Ala Asp Lys Pro Leu Ser Asn Met Lys Ile Leu Thr Leu Gly Lys	385	390	400
Leu Ser Arg Asn Lys Asp Glu Val Lys Ala Met Ile Glu Lys Leu Gly	405	410	415
Gly Lys Leu Thr Gly Thr Ala Asn Lys Ala Ser Leu Cys Ile Ser Thr	420	425	430
Lys Lys Glu Val Glu Lys Met Asn Lys Lys Met Glu Glu Val Lys Glu	435	440	445
Ala Asn Ile Arg Val Val Ser Glu Asp Phe Leu Gln Asp Val Ser Ala	450	455	460
Ser Thr Lys Ser Leu Gln Glu Leu Phe Leu Ala His Ile Leu Ser Pro	465	470	475
Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg	485	490	495
Gly Lys Ser Gly Ala Ala Leu Ser Lys Lys Ser Lys Gly Gln Val Lys	500	505	510
Glu Glu Gly Ile Asn Lys Ser Glu Lys Arg Met Lys Leu Thr Leu Lys	515	520	525
Gly Gly Ala Ala Val Asp Pro Asp Ser Gly Leu Glu His Ser Ala His	530	535	540
Val Leu Glu Lys Gly Gly Lys Val Phe Ser Ala Thr Leu Gly Leu Val	545	550	555
Asp Ile Val Lys Gly Thr Asn Ser Tyr Tyr Lys Leu Gln Leu Leu Glu	565	570	575
Asp Asp Lys Glu Asn Arg Tyr Trp Ile Phe Arg Ser Trp Gly Arg Val	580	585	590
Gly Thr Val Ile Gly Ser Asn Lys Leu Glu Gln Met Pro Ser Lys Glu	595	600	605
Asp Ala Ile Glu Gln Phe Met Lys Leu Tyr Glu Glu Lys Thr Gly Asn	610	615	620
Ala Trp His Ser Lys Asn Phe Thr Lys Tyr Pro Lys Lys Phe Tyr Pro	625	630	635
Leu Glu Ile Asp Tyr Gly Gln Asp Glu Glu Ala Val Lys Lys Leu Thr	645	650	655
Val Asn Pro Gly Thr Lys Ser Lys Leu Pro Lys Pro Val Gln Asp Leu	660	665	670
Ile Lys Met Ile Phe Asp Val Glu Ser Met Lys Lys Ala Met Val Glu	675	680	685
Tyr Glu Ile Asp Leu Gln Lys Met Pro Leu Gly Lys Leu Ser Lys Arg	690	695	700
Gln Ile Gln Ala Ala Tyr Ser Ile Leu Ser Glu Val Gln Gln Ala Val	705	710	715
Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe	725	730	735
Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu	740	745	750
Asn Asn Ala Asp Ser Val Gln Ala Lys Val Glu Met Leu Asp Asn Leu	755	760	765
Leu Asp Ile Glu Val Ala Tyr Ser Leu Leu Arg Gly Gly Ser Asp Asp	770	775	780

Ser Ser Lys Asp Pro Ile Asp Val Asn Tyr Glu Lys Leu Lys Thr Asp  
 785 790 795 800  
 Ile Lys Val Val Asp Arg Asp Ser Glu Glu Ala Glu Ile Ile Arg Lys  
 805 810 815  
 Tyr Val Lys Asn Thr His Ala Thr Thr His Ser Ala Tyr Asp Leu Glu  
 820 825 830  
 Val Ile Asp Ile Phe Lys Ile Glu Arg Glu Gly Glu Cys Gln Arg Tyr  
 835 840 845  
 Lys Pro Phe Lys Gln Leu His Asn Arg Arg Leu Leu Trp His Gly Ser  
 850 855 860  
 Arg Thr Thr Asn Phe Ala Gly Ile Leu Ser Gln Gly Leu Arg Ile Ala  
 865 870 875 880  
 Pro Pro Glu Ala Pro Val Thr Gly Tyr Met Phe Gly Lys Gly Ile Tyr  
 885 890 895  
 Phe Ala Asp Met Val Ser Lys Ser Ala Asn Tyr Tyr His Thr Ser Gln  
 900 905 910  
 Gly Asp Pro Ile Gly Leu Ile Leu Leu Gly Glu Val Ala Leu Gly Asn  
 915 920 925  
 Met Tyr Glu Leu Lys His Ala Ser His Ile Ser Arg Leu Pro Lys Gly  
 930 935 940  
 Lys His Ser Val Lys Gly Leu Gly Lys Thr Thr Pro Asp Pro Ser Ala  
 945 950 955 960  
 Asn Ile Ser Leu Asp Gly Val Asp Val Pro Leu Gly Thr Gly Ile Ser  
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 Ser Gly Val Ile Asp Thr Ser Leu Leu Tyr Asn Glu Tyr Ile Val Tyr  
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 Phe Lys Thr Ser Leu Trp  
 1010

&lt;210&gt; 5

&lt;211&gt; 1465

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 5

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 acttcggatt tcaactctacc cggagagttt cccgcttggt tgaacacatt ggcctcagga 120  
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 gagaaggacc aaaaaggaac ttgcatcagc actgaagtca gccttatctg gccacctgga 420  
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gatgtgaaac actttgcctc ctgtgtactg tgtcataaac agatgaataa actgaatttg 1440
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<210> 6
<211> 339
<212> PRT
<213> Homo sapiens

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<400> 6
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His Ser Thr Pro Pro Ser Ala Tyr Gly Ser Val Lys Ala Tyr Thr Asn
 20          25          30
Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr
 35          40          45
Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser
 50          55          60
Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys
 65          70          75          80
Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu
 85          90          95
Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser
100          105          110
Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu
115          120          125
Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn
130          135          140
Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile
145          150          155          160
Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys
165          170          175
Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp
180          185          190
Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr
195          200          205
Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His
210          215          220
Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met
225          230          235          240
Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe
245          250          255
Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp
260          265          270
Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu
275          280          285
Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg
290          295          300
Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln
305          310          315          320
Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly
325          330          335
Gly Asp Asp

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<210> 7  
 <211> 1362  
 <212> DNA  
 <213> Homo sapiens

<400> 7  
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 tgggtctgtc aaagcctata ctaactttga tgctgagcgg gatgctttga acattgaaac 180  
 agccatcaag accaaaggtg tggatgaggt caccattgtc aacattttga ccaaccgcag 240  
 caatgcacag agacaggata ttgccttcgc ctaccagaga aggacaaaaa aggaacttgc 300  
 atcagcactg aagtcagcct tatctggcca cctggagacg gtgattttgg gcctattgaa 360  
 gacacctgct cagtatgacg cttctgagct aaaagcttcc atgaaggggc tgggaaccga 420  
 cgaggactct ctcatctgaga tcatctgctc cagaaccaac caggagctgc aggaaattaa 480  
 cagagtctac aaggaaatgt acaagactga tctggagaag gacattattt cggacacatc 540  
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 cctccagaaa gtatttgata ggtacaagag ttacagccct tatgacatgt tggaaagcat 780  
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 gggcgactac cagaaagcgc tgctgtacct gtgtggtgga gatgactgaa gcccgcacacg 1080  
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 ttgcgaataa cagtccccgt ggccatccct gtgaggggtga cgttagcatt accccaacc 1200  
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 aatgaacat tccaaggagt tggaagtga gtctatgatg tgaacactt tgcctcctgt 1320  
 gtactgtgtc ataaacagat gaataaactg aatttgtact tt 1362

<210> 8  
 <211> 339  
 <212> PRT  
 <213> Homo sapiens

<400> 8  
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 His Ser Thr Pro Pro Ser Ala Tyr Gly Ser Val Lys Ala Tyr Thr Asn  
 20 25 30  
 Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr  
 35 40 45  
 Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser  
 50 55 60  
 Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys  
 65 70 75 80  
 Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu  
 85 90 95  
 Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser  
 100 105 110  
 Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu  
 115 120 125  
 Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn  
 130 135 140  
 Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile  
 145 150 155 160  
 Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys  
 165 170 175

Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp  
 180 185 190  
 Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr  
 195 200 205  
 Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His  
 210 215 220  
 Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met  
 225 230 235 240  
 Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe  
 245 250 255  
 Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp  
 260 265 270  
 Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu  
 275 280 285  
 Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg  
 290 295 300  
 Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln  
 305 310 315 320  
 Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly  
 325 330 335  
 Gly Asp Asp

&lt;210&gt; 9

&lt;211&gt; 1982

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 9

gcagaggagg agcgacgccc ggcctcgaag aactttctgct tgggtggctg aactctgac 60  
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 ctcccggacc cctgaggaga tccggcgcat aagccaaacc taccagcagc aatatggacg 480  
 gagccttgaa gatgacattc gctctgacac atcgttcatg ttccagcgag tgctggtgtc 540  
 tctgtcagct ggtgggaggg atgaaggaaa ttatctggac gatgctctcg tgagacagga 600  
 tgcccaggac ctgtatgagg ctggagagaa gaaatggggg acagatgagg tgaaatttct 660  
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 tcgagcagaa attgacatgt tggatatccg ggcacacttc aagagactct atggaaaagtc 960  
 tctgtactcg ttcattcaagg gtgacacatc tggagactac aggaaagtac tgcttgttct 1020  
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 tgtgtttcac agacattgaa tatattaaat tattccatat tttcttttca gtgaaaaatt 1380  
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 tatatttcat agtcaaagcc ttgaaagcat ctacaaatct ctttttttag gttttgtcca 1560  
 tagcatcagt tgatccttac taagttttcc atgggagact tccttcatca catcttatgt 1620  
 tgaaatcact ttctgtagtc aaagtatacc aaaaccaatt tatctgaact aaattctaaa 1680



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ctaggatttc tgggaatgat gtaatgctct gaatttagta tgatataaag aaaacttttt 1860
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&lt;210&gt; 10

&lt;211&gt; 321

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

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Met Ala Met Ala Thr Lys Gly Gly Thr Val Lys Ala Ala Ser Gly Phe
  1          5          10          15
Asn Ala Met Glu Asp Ala Gln Thr Leu Arg Lys Ala Met Lys Gly Leu
  20          25          30
Gly Thr Asp Glu Asp Ala Ile Ile Ser Val Leu Ala Tyr Arg Asn Thr
  35          40          45
Ala Gln Arg Gln Glu Ile Arg Thr Ala Tyr Lys Ser Thr Ile Gly Arg
  50          55          60
Asp Leu Ile Asp Asp Leu Lys Ser Glu Leu Ser Gly Asn Phe Glu Gln
  65          70          75          80
Val Ile Val Gly Met Met Thr Pro Thr Val Leu Tyr Asp Val Gln Glu
  85          90          95
Leu Arg Arg Ala Met Lys Gly Ala Gly Thr Asp Glu Gly Cys Leu Ile
  100         105         110
Glu Ile Leu Ala Ser Arg Thr Pro Glu Glu Ile Arg Arg Ile Ser Gln
  115         120         125
Thr Tyr Gln Gln Gln Tyr Gly Arg Ser Leu Glu Asp Asp Ile Arg Ser
  130         135         140
Asp Thr Ser Phe Met Phe Gln Arg Val Leu Val Ser Leu Ser Ala Gly
  145         150         155         160
Gly Arg Asp Glu Gly Asn Tyr Leu Asp Asp Ala Leu Val Arg Gln Asp
  165         170         175
Ala Gln Asp Leu Tyr Glu Ala Gly Glu Lys Lys Trp Gly Thr Asp Glu
  180         185         190
Val Lys Phe Leu Thr Val Leu Cys Ser Arg Asn Arg Asn His Leu Leu
  195         200         205
His Val Phe Asp Glu Tyr Lys Arg Ile Ser Gln Lys Asp Ile Glu Gln
  210         215         220
Ser Ile Lys Ser Glu Thr Ser Gly Ser Phe Glu Asp Ala Leu Leu Ala
  225         230         235         240
Ile Val Lys Cys Met Arg Asn Lys Ser Ala Tyr Phe Ala Glu Lys Leu
  245         250         255
Tyr Lys Ser Met Lys Gly Leu Gly Thr Asp Asp Asn Thr Leu Ile Arg
  260         265         270
Val Met Val Ser Arg Ala Glu Ile Asp Met Leu Asp Ile Arg Ala His
  275         280         285
Phe Lys Arg Leu Tyr Gly Lys Ser Leu Tyr Ser Phe Ile Lys Gly Asp
  290         295         300
Thr Ser Gly Asp Tyr Arg Lys Val Leu Leu Val Leu Cys Gly Gly Asp
  305         310         315         320
Asp

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&lt;210&gt; 11

<211> 1316  
 <212> DNA  
 <213> Homo sapiens

<400> 11  
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 cgggacgctg ggccgttcta caccgcccgc tgggtcacgt ggcccggaag ggccggcgcc 180  
 tgccccggcc gggggcggg ggtcgcgccg gggttgcgct ggacgacgga gagcggcggg 240  
 cccgcagcgg cctggagcct cccaaccgc gccgcgtgg ccctcgagcg taggagccgc 300  
 cccctgcccc ccgcgcggg ccccgcgccc ggccgcccgc ccctatata gcgcgcccc 360  
 gcagggcccc cgccaggccg ccagcctcgg agtgggcgcg ggacagtgcg cggcgccccg 420  
 cagccaggcc ccgcggccg ccgcatccac ctccctcgcc gcctgcgacc caacgggccc 480  
 cccccgcccg cagctcgcg cgggccccg cgccaccat gaagaaggag gtgtgctccg 540  
 tggccttcct caaggccgtg ttgcagagt tcttgccac cctcatcttc gtcttctttg 600  
 gcctgggctc ggccctcaag tggcgtcgg cgctgcctac catcctgcag atcgcgctgg 660  
 cgcttgccct ggccataggc acgctggccc aggccttggg acccgtgagc ggccggccaca 720  
 tcaacccgc catcaccctg gccctcttgg tgggcaacca gatctcgctg ctccgggctt 780  
 tcttctacgt ggcgcccag ctggtggcg ccattgccc ggctggcatc ctctacgggtg 840  
 tggcaccgct caatgcccgg ggcaatctgg ccgtcaacgc gctcaacaac aacacaacgc 900  
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 gctcttttgg cctgcccgtg gtcatgaatc ggttcagccc cgctcactgg gttttctggg 1140  
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 actgggagga gcagcgggaa gagcggaaga agaccatgga gctgaccacc cgctga 1316

<210> 12  
 <211> 265  
 <212> PRT  
 <213> Homo sapiens

<400> 12  
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 20 25 30  
 Leu Lys Trp Pro Ser Ala Leu Pro Thr Ile Leu Gln Ile Ala Leu Ala  
 35 40 45  
 Phe Gly Leu Ala Ile Gly Thr Leu Ala Gln Ala Leu Gly Pro Val Ser  
 50 55 60  
 Gly Gly His Ile Asn Pro Ala Ile Thr Leu Ala Leu Leu Val Gly Asn  
 65 70 75 80  
 Gln Ile Ser Leu Leu Arg Ala Phe Phe Tyr Val Ala Ala Gln Leu Val  
 85 90 95  
 Gly Ala Ile Ala Gly Ala Gly Ile Leu Tyr Gly Val Ala Pro Leu Asn  
 100 105 110  
 Ala Arg Gly Asn Leu Ala Val Asn Ala Leu Asn Asn Asn Thr Thr Gln  
 115 120 125  
 Gly Gln Ala Met Val Val Glu Leu Ile Leu Thr Phe Gln Leu Ala Leu  
 130 135 140  
 Cys Ile Phe Ala Ser Thr Asp Ser Arg Arg Thr Ser Pro Val Gly Ser  
 145 150 155 160  
 Pro Ala Leu Ser Ile Gly Leu Ser Val Thr Leu Gly His Leu Val Gly  
 165 170 175  
 Ile Tyr Phe Thr Gly Cys Ser Met Asn Pro Ala Arg Ser Phe Gly Pro  
 180 185 190

Ala Val Val Met Asn Arg Phe Ser Pro Ala His Trp Val Phe Trp Val  
 195 200 205  
 Gly Pro Ile Val Gly Ala Val Leu Ala Ala Ile Leu Tyr Phe Tyr Leu  
 210 215 220  
 Leu Phe Pro Asn Ser Leu Ser Leu Ser Glu Arg Val Ala Ile Ile Lys  
 225 230 235 240  
 Gly Thr Tyr Glu Pro Asp Glu Asp Trp Glu Glu Gln Arg Glu Glu Arg  
 245 250 255  
 Lys Lys Thr Met Glu Leu Thr Thr Arg  
 260 265

<210> 13  
 <211> 1653  
 <212> DNA  
 <213> Homo sapiens

<400> 13  
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 ccgtggccag agctgcagag agacaaggcg gcggcggctg ctgtgctggg tgcagtgagg 120  
 aagaggccct cgggtgggtgcc catggctggc caggatcctg cgctgagcac gagtaccccg 180  
 ttctacgacg tggccagaca tggcattctg caggtggcag gggatgaccg ctttgaaga 240  
 cgtgttgta cgttcagctg ctgccggatg ccgccctccc acgagctgga ccaccagcgg 300  
 ctgctggagt atttgaagta cactactggac caatacgttg agaacgatta taccatcgtc 360  
 tatttccact acgggctgaa cagccggaac aagccttccc tgggctggct ccagagcgca 420  
 tacaaggagt tcgataggaa agacggggat ctactatgt ggcccaggct ggtctcgaac 480  
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 aagaacttga aggccttcta cgtggtgcac cccaccagct tcatcaaggc cctgtggaac 600  
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 agtgagctcc acgaacacct taaatacgac cagctgggtca tccctcccga agttttgcgg 720  
 tacgatgaga agctccagag cctgcacgag ggccggacgc cgctcctac caagacacca 780  
 ccgcccgggc ccccgctgcc cacacagcag tttggcgtca gtctgcaata cctcaaagac 840  
 aaaaatcaag gcgaactcat cccccctgtg ctgaggttca cagtgcgta cctgagagag 900  
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 caggcctacg agcagattct cgggatcacc tgtgtggaga gcagcctgcg tgtcactggc 1140  
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 ggctttctgc atgcggtgtc ccgggagagc atcttcaaca aaatgaacag ctctaaccgt 1260  
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 cttgtgcccc tgaacatgtt cactgaactg ctgatcgagt actatgaaaa gatcttcagc 1380  
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 cctttgcagg aggtgtgcc acggacacaa gccacgggcc tcaccaagcc taccctacct 1500  
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 ataaccagcc attagatgaa ttcagaacct tct 1653

<210> 14  
 <211> 464  
 <212> PRT  
 <213> Homo sapiens

<400> 14  
 Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp  
 1 5 10 15  
 Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly  
 20 25 30

Arg	Arg	Val	Val	Thr	Phe	Ser	Cys	Cys	Arg	Met	Pro	Pro	Ser	His	Glu
		35					40					45			
Leu	Asp	His	Gln	Arg	Leu	Leu	Glu	Tyr	Leu	Lys	Tyr	Thr	Leu	Asp	Gln
	50					55					60				
Tyr	Val	Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly	Leu	Asn
65					70					75					80
Ser	Arg	Asn	Lys	Pro	Ser	Leu	Gly	Trp	Leu	Gln	Ser	Ala	Tyr	Lys	Glu
			85						90					95	
Phe	Asp	Arg	Lys	Asp	Gly	Asp	Leu	Thr	Met	Trp	Pro	Arg	Leu	Val	Ser
			100					105						110	
Asn	Ser	Lys	Leu	Lys	Arg	Ser	Ser	His	Leu	Ser	Leu	Pro	Lys	Tyr	Trp
		115					120					125			
Asp	Tyr	Arg	Tyr	Lys	Lys	Asn	Leu	Lys	Ala	Leu	Tyr	Val	Val	His	Pro
	130					135					140				
Thr	Ser	Phe	Ile	Lys	Val	Leu	Trp	Asn	Ile	Leu	Lys	Pro	Leu	Ile	Ser
145					150					155					160
His	Lys	Phe	Gly	Lys	Lys	Val	Ile	Tyr	Phe	Asn	Tyr	Leu	Ser	Glu	Leu
			165						170					175	
His	Glu	His	Leu	Lys	Tyr	Asp	Gln	Leu	Val	Ile	Pro	Pro	Glu	Val	Leu
			180					185						190	
Arg	Tyr	Asp	Glu	Lys	Leu	Gln	Ser	Leu	His	Glu	Gly	Arg	Thr	Pro	Pro
		195					200					205			
Pro	Thr	Lys	Thr	Pro	Pro	Pro	Arg	Pro	Pro	Leu	Pro	Thr	Gln	Gln	Phe
	210					215					220				
Gly	Val	Ser	Leu	Gln	Tyr	Leu	Lys	Asp	Lys	Asn	Gln	Gly	Glu	Leu	Ile
225					230					235					240
Pro	Pro	Val	Leu	Arg	Phe	Thr	Val	Thr	Tyr	Leu	Arg	Glu	Lys	Gly	Leu
			245						250					255	
Arg	Thr	Glu	Gly	Leu	Phe	Arg	Arg	Ser	Ala	Ser	Val	Gln	Thr	Val	Arg
		260						265						270	
Glu	Ile	Gln	Arg	Leu	Tyr	Asn	Gln	Gly	Lys	Pro	Val	Asn	Phe	Asp	Asp
		275				280						285			
Tyr	Gly	Asp	Ile	His	Ile	Pro	Ala	Val	Ile	Leu	Lys	Thr	Phe	Leu	Arg
	290					295					300				
Glu	Leu	Pro	Gln	Pro	Leu	Leu	Thr	Phe	Gln	Ala	Tyr	Glu	Gln	Ile	Leu
305					310					315					320
Gly	Ile	Thr	Cys	Val	Glu	Ser	Ser	Leu	Arg	Val	Thr	Gly	Cys	Arg	Gln
			325						330					335	
Ile	Leu	Arg	Ser	Leu	Pro	Glu	His	Asn	Tyr	Val	Val	Leu	Arg	Tyr	Leu
		340						345					350		
Met	Gly	Phe	Leu	His	Ala	Val	Ser	Arg	Glu	Ser	Ile	Phe	Asn	Lys	Met
		355					360					365			
Asn	Ser	Ser	Asn	Leu	Ala	Cys	Val	Phe	Gly	Leu	Asn	Leu	Ile	Trp	Pro
	370					375					380				
Ser	Gln	Gly	Val	Ser	Ser	Leu	Ser	Ala	Leu	Val	Pro	Leu	Asn	Met	Phe
385					390					395					400
Thr	Glu	Leu	Leu	Ile	Glu	Tyr	Tyr	Glu	Lys	Ile	Phe	Ser	Thr	Pro	Glu
			405						410					415	
Ala	Pro	Gly	Glu	His	Gly	Leu	Ala	Pro	Trp	Glu	Gln	Gly	Ser	Arg	Ala
		420						425					430		
Ala	Pro	Leu	Gln	Glu	Ala	Val	Pro	Arg	Thr	Gln	Ala	Thr	Gly	Leu	Thr
	435						440					445			
Lys	Pro	Thr	Leu	Pro	Pro	Ser	Pro	Leu	Met	Ala	Ala	Arg	Arg	Arg	Leu
	450					455					460				

&lt;210&gt; 15

&lt;211&gt; 2043

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 15

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gaa
2043

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&lt;210&gt; 16

&lt;211&gt; 643

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 16

```

Met Arg Thr Leu Arg Arg Leu Lys Phe Met Ser Ser Pro Ser Leu Ser
1           5           10           15
Asp Leu Gly Lys Arg Glu Pro Ala Ala Ala Asp Glu Arg Gly Thr
20           25           30
Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35           40           45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50           55           60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65           70           75           80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85           90           95

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Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu  
 100 105 110  
 Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro  
 115 120 125  
 Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val  
 130 135 140  
 Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val  
 145 150 155 160  
 Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala  
 165 170 175  
 Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly  
 180 185 190  
 Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val  
 195 200 205  
 Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe  
 210 215 220  
 Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala  
 225 230 235 240  
 Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala  
 245 250 255  
 Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala  
 260 265 270  
 Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg  
 275 280 285  
 Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp  
 290 295 300  
 His Gln Arg Leu Leu Glu Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val  
 305 310 315 320  
 Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro  
 325 330 335  
 Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu  
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 Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro  
 355 360 365  
 Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg  
 370 375 380  
 Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr  
 385 390 395 400  
 Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly  
 405 410 415  
 Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu  
 420 425 430  
 Lys Gly Leu Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln  
 435 440 445  
 Thr Val Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn  
 450 455 460  
 Phe Asp Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr  
 465 470 475 480  
 Phe Leu Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu  
 485 490 495  
 Gln Ile Leu Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly  
 500 505 510  
 Cys Arg Gln Ile Leu Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu  
 515 520 525  
 Arg Tyr Leu Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe  
 530 535 540  
 Asn Lys Met Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu  
 545 550 555 560

Ile Trp Pro Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu  
 565 570 575  
 Asn Met Phe Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser  
 580 585 590  
 Thr Pro Glu Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly  
 595 600 605  
 Ser Arg Ala Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr  
 610 615 620  
 Gly Leu Thr Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg  
 625 630 635 640  
 Arg Arg Leu

&lt;210&gt; 17

&lt;211&gt; 2274

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 17

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gagaacgatt ataccatcgt ctatttccac tacgggctga acagccgaa caagccttcc 1020
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<210> 18  
 <211> 751  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> (1)...(751)  
 <223> Xaa = Any Amino Acid

<400> 18

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Asp	Leu	Gly	Lys	Arg	Glu	Pro	Ala	Ala	Ala	Ala	Asp	Glu	Arg	Gly	Thr
		20					25					30			
Gln	Gln	Arg	Arg	Ala	Cys	Ala	Asn	Ala	Thr	Trp	Asn	Ser	Ile	His	Asn
		35					40					45			
Gly	Val	Ile	Ala	Val	Phe	Gln	Arg	Lys	Gly	Leu	Pro	Asp	Gln	Glu	Leu
	50					55					60				
Phe	Ser	Leu	Asn	Glu	Gly	Val	Arg	Gln	Leu	Leu	Lys	Thr	Glu	Leu	Gly
65				70					75					80	
Ser	Phe	Phe	Thr	Glu	Tyr	Leu	Gln	Asn	Gln	Leu	Leu	Thr	Lys	Gly	Met
			85					90						95	
Val	Ile	Leu	Arg	Asp	Lys	Ile	Arg	Phe	Tyr	Glu	Gly	Gln	Lys	Leu	Leu
		100						105					110		
Asp	Ser	Leu	Ala	Glu	Thr	Trp	Asp	Phe	Phe	Phe	Ser	Asp	Val	Leu	Pro
		115					120					125			
Met	Leu	Gln	Ala	Ile	Phe	Tyr	Pro	Val	Gln	Gly	Lys	Glu	Pro	Ser	Val
	130					135					140				
Arg	Gln	Leu	Ala	Leu	Leu	His	Phe	Arg	Asn	Ala	Ile	Thr	Leu	Ser	Val
145				150						155				160	
Lys	Leu	Glu	Asp	Ala	Leu	Ala	Arg	Ala	His	Ala	Arg	Val	Pro	Pro	Ala
			165					170						175	
Ile	Val	Gln	Met	Leu	Leu	Val	Leu	Gln	Gly	Val	His	Glu	Ser	Arg	Gly
		180						185					190		
Val	Thr	Glu	Asp	Tyr	Leu	Arg	Leu	Glu	Thr	Leu	Val	Gln	Lys	Val	Val
	195						200					205			
Ser	Pro	Tyr	Leu	Gly	Thr	Tyr	Gly	Leu	His	Ser	Ser	Glu	Gly	Pro	Phe
	210					215					220				
Thr	His	Ser	Cys	Ile	Leu	Glu	Leu	Gln	Arg	Asp	Lys	Ala	Ala	Ala	Ala
225				230						235				240	
Ala	Val	Leu	Gly	Ala	Val	Arg	Lys	Arg	Pro	Ser	Val	Val	Pro	Met	Ala
			245						250					255	
Gly	Gln	Asp	Pro	Ala	Leu	Ser	Thr	Ser	His	Pro	Phe	Tyr	Asp	Val	Ala
		260						265					270		
Arg	His	Gly	Ile	Leu	Gln	Val	Ala	Gly	Asp	Asp	Arg	Phe	Gly	Arg	Arg
	275						280					285			
Val	Val	Thr	Phe	Ser	Cys	Cys	Arg	Met	Pro	Pro	Ser	His	Glu	Leu	Asp
	290					295					300				
His	Gln	Arg	Leu	Leu	Glu	Tyr	Leu	Lys	Tyr	Thr	Leu	Asp	Gln	Tyr	Val
305				310						315				320	
Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly	Leu	Asn	Ser	Arg
			325						330					335	
Asn	Lys	Pro	Ser	Leu	Gly	Trp	Leu	Gln	Ser	Ala	Tyr	Lys	Glu	Phe	Asp
		340						345					350		
Arg	Lys	Asp	Gly	Asp	Leu	Thr	Met	Trp	Pro	Arg	Leu	Val	Ser	Asn	Ser
		355					360					365			



Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr  
 370 375 380  
 Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser  
 385 390 395 400  
 Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys  
 405 410 415  
 Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu  
 420 425 430  
 His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr  
 435 440 445  
 Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr  
 450 455 460  
 Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val  
 465 470 475 480  
 Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro  
 485 490 495  
 Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Arg Thr  
 500 505 510  
 Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile  
 515 520 525  
 Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp Tyr Gly  
 530 535 540  
 Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg Glu Leu  
 545 550 555 560  
 Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu Gly Ile  
 565 570 575  
 Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln Ile Leu  
 580 585 590  
 Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly  
 595 600 605  
 Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser  
 610 615 620  
 Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln  
 625 630 635 640  
 Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu  
 645 650 655  
 Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro  
 660 665 670  
 Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro  
 675 680 685  
 Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro  
 690 695 700  
 Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu Xaa Cys  
 705 710 715 720  
 Cys Glu His Ser Val Tyr Phe Glu Leu Pro Pro Thr Pro Val Cys Ala  
 725 730 735  
 Leu Val Cys Phe Val Asn Leu Ala Ser Val Lys Ile Thr Ser His  
 740 745 750

&lt;210&gt; 19

&lt;211&gt; 718

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

Met Arg Thr Leu Arg Arg Leu Lys Phe Met Ser Ser Pro Ser Leu Ser  
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Asp Leu Gly Lys Arg Glu Pro Ala Ala Ala Asp Glu Arg Gly Thr  
 20 25 30  
 Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn  
 35 40 45  
 Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu  
 50 55 60  
 Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly  
 65 70 75 80  
 Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met  
 85 90 95  
 Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu  
 100 105 110  
 Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro  
 115 120 125  
 Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val  
 130 135 140  
 Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val  
 145 150 155 160  
 Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala  
 165 170 175  
 Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly  
 180 185 190  
 Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val  
 195 200 205  
 Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe  
 210 215 220  
 Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala  
 225 230 235 240  
 Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala  
 245 250 255  
 Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala  
 260 265 270  
 Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg  
 275 280 285  
 Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp  
 290 295 300  
 His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln Tyr Val  
 305 310 315 320  
 Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn Ser Arg  
 325 330 335  
 Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu Phe Asp  
 340 345 350  
 Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser Asn Ser  
 355 360 365  
 Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr  
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 Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser  
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 Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu  
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 Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr  
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 Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val  
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 Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile  
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 530 535 540  
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 545 550 555 560  
 Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu Gly Ile  
 565 570 575  
 Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln Ile Leu  
 580 585 590  
 Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly  
 595 600 605  
 Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser  
 610 615 620  
 Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln  
 625 630 635 640  
 Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu  
 645 650 655  
 Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro  
 660 665 670  
 Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro  
 675 680 685  
 Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro  
 690 695 700  
 Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu  
 705 710 715

&lt;210&gt; 20

&lt;211&gt; 1431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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 ctgctggaca ggtacaagaa gaacttgaag gccctctacg tgggtgcaccc caccagcttc 360  
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 cctcccacca agacaccacc gccgcggccc ccgctgccc caccagcagtt tggcgtcagt 600  
 ctgcaatacc tcaaagacaa aaatcaaggc gaactcatcc cccctgtgct gaggttcaca 660  
 gtgacgtacc tgagagagaa aggctgccc accgagggcc tgttccggag atccgccagc 720  
 gtgcagaccg tccgcgagat ccagaggctc tacaaccaag ggaagcccgt gaactttgac 780  
 gactacgggg acattcacat ccctgccgtg atcctgaaga ccttcctgcg agagctgccc 840  
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Glu	Gln	Gly	Ser	Arg	Ala	Ala	Pro	Leu	Gln	Glu	Ala	Val	Pro	Arg	Thr	355		360		365		
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Met	Leu	Gln	Ala	Ile	Phe	Tyr	Pro	Val	Gln	Gly	Lys	Glu	Pro	Ser	Val	130	135	140
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Lys	Leu	Glu	Asp	Ala	Leu	Ala	Arg	Ala	His	Ala	Arg	Val	Pro	Pro	Ala	165	170	175
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Tyr	Val	Glu	Asn	Asp	Tyr	Thr	Ile	Val	Tyr	Phe	His	Tyr	Gly
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&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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&lt;210&gt; 27

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

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50          55          60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
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Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85          90          95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
100          105          110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
115          120          125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
130          135          140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145          150          155          160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
165          170          175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
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Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
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 Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala  
 260 265 270  
 Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg  
 275 280 285  
 Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp  
 290 295 300  
 His Gln Arg Leu Leu Glu Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val  
 305 310 315 320  
 Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro  
 325 330 335  
 Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu  
 340 345 350  
 Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro  
 355 360 365  
 Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg  
 370 375 380  
 Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr  
 385 390 395 400  
 Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly  
 405 410 415  
 Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu  
 420 425 430  
 Lys Ala Ser Gln Ser Thr Thr Thr Ser Ser Ala Thr Ser Trp Ala  
 435 440 445  
 Ser Cys Met Arg Cys Pro Gly Arg Ala Ser Ser Thr Lys  
 450 455 460

&lt;210&gt; 28

&lt;211&gt; 1176

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

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 <211> 305  
 <212> PRT  
 <213> Homo sapiens

<400> 29  
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 Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu  
 35 40 45  
 Leu Asp His Gln Arg Leu Leu Asp Arg Tyr Lys Lys Asn Leu Lys Ala  
 50 55 60  
 Leu Tyr Val Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile  
 65 70 75 80  
 Leu Lys Pro Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe  
 85 90 95  
 Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val  
 100 105 110  
 Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His  
 115 120 125  
 Glu Gly Arg Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro  
 130 135 140  
 Leu Pro Thr Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys  
 145 150 155 160  
 Asn Gln Gly Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr  
 165 170 175  
 Leu Arg Glu Lys Gly Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr  
 180 185 190  
 Leu Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys  
 195 200 205  
 Met Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp  
 210 215 220  
 Pro Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met  
 225 230 235 240  
 Phe Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro  
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 Glu Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg  
 260 265 270  
 Ala Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu  
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 Leu  
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 <213> Homo sapiens

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&lt;210&gt; 31

&lt;211&gt; 975

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 31.

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Ile	Glu	Arg	Leu	Thr	Lys	Glu	Leu	Thr	Glu	Thr	Thr	His	Glu	Lys	Ile
		20						25					30		
Gln	Ala	Ala	Glu	Tyr	Gly	Leu	Val	Val	Leu	Glu	Glu	Lys	Leu	Thr	Leu
		35					40					45			
Lys	Gln	Gln	Tyr	Asp	Glu	Leu	Glu	Ala	Glu	Tyr	Asp	Ser	Leu	Lys	Gln
	50					55					60				
Glu	Leu	Glu	Gln	Leu	Lys	Glu	Ala	Phe	Gly	Gln	Ser	Phe	Ser	Ile	His
65.					70					75					80
Arg	Lys	Val	Ala	Glu	Asp	Gly	Glu	Thr	Arg	Glu	Glu	Thr	Leu	Leu	Gln
			85						90					95	
Glu	Ser	Ala	Ser	Lys	Glu	Ala	Tyr	Tyr	Leu	Gly	Lys	Ile	Leu	Glu	Met
		100						105					110		
Gln	Asn	Glu	Leu	Lys	Gln	Ser	Arg	Ala	Val	Val	Thr	Asn	Val	Gln	Ala
	115						120					125			
Glu	Asn	Glu	Arg	Leu	Thr	Ala	Val	Val	Gln	Asp	Leu	Lys	Glu	Asn	Asn
	130					135					140				
Glu	Met	Val	Glu	Leu	Gln	Arg	Ile	Arg	Met	Lys	Asp	Glu	Ile	Arg	Glu
145					150					155					160
Tyr	Lys	Phe	Arg	Glu	Ala	Arg	Leu	Leu	Gln	Asp	Tyr	Thr	Glu	Leu	Glu
			165						170					175	
Glu	Glu	Asn	Ile	Thr	Leu	Gln	Lys	Leu	Val	Ser	Thr	Leu	Lys	Gln	Asn
		180						185					190		
Gln	Val	Glu	Tyr	Glu	Gly	Leu	Lys	His	Glu	Ile	Lys	Arg	Phe	Glu	Glu
	195						200					205			
Glu	Thr	Val	Leu	Leu	Asn	Ser	Gln	Leu	Glu	Asp	Ala	Ile	Arg	Leu	Lys
	210				215						220				
Glu	Ile	Ala	Glu	His	Gln	Leu	Glu	Glu	Ala	Leu	Glu	Thr	Leu	Lys	Asn
225					230					235					240
Glu	Arg	Glu	Gln	Lys	Asn	Asn	Leu	Arg	Lys	Glu	Leu	Ser	Gln	Tyr	Ile
			245						250					255	
Ser	Leu	Asn	Asp	Asn	His	Ile	Ser	Ile	Ser	Val	Asp	Gly	Leu	Lys	Phe
		260						265					270		
Ala	Glu	Asp	Gly	Ser	Glu	Pro	Asn	Asn	Asp	Asp	Lys	Met	Asn	Gly	His
		275					280					285			
Ile	His	Gly	Pro	Leu	Val	Lys	Leu	Asn	Gly	Asp	Tyr	Arg	Thr	Pro	Thr
	290					295					300				
Leu	Arg	Lys	Gly	Glu	Ser	Leu	Asn	Pro	Val	Ser	Asp	Leu	Phe	Ser	Glu
305					310					315					320
Leu	Asn	Ile	Ser	Glu	Ile	Gln	Lys	Leu	Lys	Gln	Gln	Leu	Met	Gln	Val
			325						330					335	
Glu	Arg	Glu	Lys	Ala	Ile	Leu	Leu	Ala	Asn	Leu	Gln	Glu	Ser	Gln	Thr
		340						345					350		
Gln	Leu	Glu	His	Thr	Lys	Gly	Ala	Leu	Thr	Glu	Gln	His	Glu	Arg	Val
	355						360					365			
His	Arg	Leu	Thr	Glu	His	Val	Asn	Ala	Met	Arg	Gly	Leu	Gln	Ser	Ser
	370				375						380				
Lys	Glu	Leu	Lys	Ala	Glu	Leu	Asp	Gly	Glu	Lys	Gly	Arg	Asp	Ser	Gly
385					390					395					400
Glu	Glu	Ala	His	Asp	Tyr	Glu	Val	Asp	Ile	Asn	Gly	Leu	Glu	Ile	Leu
			405						410					415	
Glu	Cys	Lys	Tyr	Arg	Val	Ala	Val	Thr	Glu	Val	Ile	Asp	Leu	Lys	Ala
			420					425				430			
Glu	Ile	Lys	Ala	Leu	Lys	Glu	Lys	Tyr	Asn	Lys	Ser	Val	Glu	Asn	Tyr

435					440					445					
Thr	Asp	Glu	Lys	Ala	Lys	Tyr	Glu	Ser	Lys	Ile	Gln	Met	Tyr	Asp	Glu
450						455					460				
Gln	Val	Thr	Ser	Leu	Glu	Lys	Thr	Thr	Lys	Glu	Ser	Gly	Glu	Lys	Met
465				470						475					480
Ala	His	Met	Glu	Lys	Glu	Leu	Gln	Lys	Met	Thr	Ser	Ile	Ala	Asn	Glu
				485					490					495	
Asn	His	Ser	Thr	Leu	Asn	Thr	Ala	Gln	Asp	Glu	Leu	Val	Thr	Phe	Ser
		500						505					510		
Glu	Glu	Leu	Ala	Gln	Leu	Tyr	His	His	Val	Cys	Leu	Cys	Asn	Asn	Glu
		515					520					525			
Thr	Pro	Asn	Arg	Val	Met	Leu	Asp	Tyr	Tyr	Arg	Gln	Ser	Arg	Val	Thr
530						535					540				
Arg	Ser	Gly	Ser	Leu	Lys	Gly	Pro	Asp	Asp	Pro	Arg	Gly	Leu	Leu	Ser
545					550					555					560
Pro	Arg	Leu	Ala	Arg	Arg	Gly	Val	Ser	Ser	Pro	Val	Glu	Thr	Arg	Thr
				565					570					575	
Ser	Ser	Glu	Pro	Val	Ala	Lys	Glu	Ser	Thr	Glu	Pro	Ser	Lys	Glu	Pro
			580						585				590		
Ser	Pro	Thr	Lys	Thr	Pro	Thr	Ile	Ser	Pro	Val	Ile	Thr	Ala	Pro	Pro
		595					600					605			
Ser	Ser	Pro	Val	Leu	Asp	Thr	Ser	Asp	Ile	Arg	Lys	Glu	Pro	Met	Asn
610						615					620				
Ile	Tyr	Asn	Leu	Asn	Ala	Ile	Ile	Arg	Asp	Gln	Ile	Lys	His	Leu	Gln
625					630					635					640
Lys	Ala	Val	Asp	Arg	Ser	Leu	Gln	Leu	Ser	Arg	Gln	Arg	Ala	Ala	Ala
				645						650				655	
Arg	Glu	Leu	Ala	Pro	Met	Ile	Asp	Lys	Asp	Lys	Glu	Ala	Leu	Met	Glu
			660						665				670		
Glu	Ile	Leu	Lys	Leu	Lys	Ser	Leu	Leu	Ser	Thr	Lys	Arg	Glu	Gln	Ile
		675					680					685			
Ala	Thr	Leu	Arg	Ala	Val	Leu	Lys	Ala	Asn	Lys	Gln	Thr	Ala	Glu	Val
690						695					700				
Ala	Leu	Ala	Asn	Leu	Lys	Asn	Lys	Tyr	Glu	Asn	Glu	Lys	Ala	Met	Val
705					710					715					720
Thr	Glu	Thr	Met	Thr	Lys	Leu	Arg	Asn	Glu	Leu	Lys	Ala	Leu	Lys	Glu
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Asp	Ala	Ala	Thr	Phe	Ser	Ser	Leu	Arg	Thr	Met	Phe	Ala	Thr	Arg	Cys
			740						745				750		
Asp	Glu	Tyr	Val	Thr	Gln	Leu	Asp	Glu	Met	Gln	Arg	Gln	Leu	Ala	Ala
		755					760					765			
Ala	Glu	Asp	Glu	Lys	Lys	Thr	Leu	Asn	Thr	Leu	Leu	Arg	Met	Ala	Ile
770						775					780				
Gln	Gln	Lys	Leu	Ala	Leu	Thr	Gln	Arg	Leu	Glu	Asp	Leu	Glu	Phe	Asp
785					790						795				800
His	Glu	Gln	Ser	Arg	Arg	Ser	Lys	Gly	Lys	Leu	Gly	Lys	Ser	Lys	Ile
				805					810					815	
Gly	Ser	Pro	Lys	Val	Ser	Gly	Glu	Ala	Ser	Val	Thr	Val	Pro	Thr	Ile
			820						825				830		
Asp	Thr	Tyr	Leu	Leu	His	Ser	Gln	Gly	Pro	Gln	Thr	Pro	Asn	Ile	Arg
		835					840						845		
Val	Ser	Ser	Gly	Thr	Gln	Arg	Lys	Arg	Gln	Phe	Ser	Pro	Ser	Leu	Cys
850						855					860				
Asp	Gln	Ser	Arg	Pro	Arg	Thr	Ser	Gly	Ala	Ser	Tyr	Leu	Gln	Asn	Leu
865					870					875					880
Leu	Arg	Val	Pro	Pro	Asp	Pro	Thr	Ser	Thr	Glu	Ser	Phe	Leu	Leu	Lys
				885					890					895	
Gly	Pro	Pro	Ser	Met	Ser	Glu	Phe	Ile	Gln	Gly	His	Arg	Leu	Ser	Lys

	900		905		910
Glu Lys Arg	Leu Thr Val Ala Pro	Pro Asp Cys	Gln Gln Pro	Ala Ala	
	915	920	925		
Ser Val Pro	Pro Gln Cys Ser Gln	Leu Ala Gly	Arg Gln Asp	Cys Pro	
	930	935	940		
Thr Val Ser	Pro Asp Thr Ala Leu	Pro Glu Glu	Gln Pro His	Ser Ser	
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Ser Gln Cys	Ala Pro Leu His Cys	Leu Ser Lys	Pro Pro His	Pro	
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<210> 32  
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 <212> DNA  
 <213> Homo sapiens

<400> 32  
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&lt;210&gt; 33

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 33

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Met Ser His Gly Lys Gly Thr Asp Met Leu Pro Glu Ile Ala Ala Ala
1          5          10          15
Val Gly Phe Leu Ser Ser Leu Leu Arg Thr Arg Gly Cys Val Ser Glu
20          25          30
Gln Arg Leu Lys Val Phe Ser Gly Ala Leu Gln Glu Ala Leu Thr Glu
35          40          45
His Tyr Lys His His Trp Phe Pro Glu Lys Pro Ser Lys Gly Ser Gly
50          55          60
Tyr Arg Cys Ile Arg Ile Asn His Lys Met Asp Pro Ile Ile Ser Arg
65          70          75          80
Val Ala Ser Gln Ile Gly Leu Ser Gln Pro Gln Leu His Gln Leu Leu
85          90          95
Pro Ser Glu Leu Thr Leu Trp Val Asp Pro Tyr Glu Val Ser Tyr Arg
100         105         110
Ile Gly Glu Asp Gly Ser Ile Cys Val Leu Tyr Glu Glu Ala Pro Leu
115         120         125
Ala Ala Ser Cys Gly Leu Leu Thr Cys Lys Asn Gln Val Leu Leu Gly
130         135         140
Arg Ser Ser Pro Ser Lys Asn Tyr Val Met Ala Val Ser Ser
145         150         155

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&lt;210&gt; 34

&lt;211&gt; 5471

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 34

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&lt;210&gt; 35

&lt;211&gt; 1390

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 35

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Ala Pro Pro Thr Phe Cys Thr Pro Ser Arg Gly Leu Gln Arg Pro Arg
20      25      30
Ser Pro Gly Ala Thr Met Leu Asp Pro Ser Ser Ser Glu Glu Glu Ser
35      40      45
Asp Glu Ile Val Glu Glu Glu Ser Gly Lys Glu Val Leu Gly Ser Ala
50      55      60
Pro Ser Gly Ala Arg Leu Ser Pro Ser Arg Thr Ser Glu Gly Ser Ala
65      70      75      80
Gly Ser Ala Gly Leu Gly Gly Gly Gly Ala Gly Ala Gly Ala Gly Val
85      90      95
Gly Ala Gly Gly Gly Gly Gly Ser Gly Ala Ser Ser Gly Gly Gly Ala
100     105     110
Gly Gly Leu Gln Pro Ser Ser Arg Ala Gly Gly Gly Arg Pro Ser Ser
115     120     125
Pro Ser Pro Ser Val Val Ser Glu Lys Glu Lys Glu Glu Leu Glu Arg
130     135     140
Leu Gln Lys Glu Glu Glu Glu Arg Lys Lys Arg Leu Gln Leu Tyr Val
145     150     155     160
Phe Val Met Arg Cys Ile Ala Tyr Pro Phe Asn Ala Lys Gln Pro Thr
165     170     175
Asp Met Ala Arg Arg Gln Gln Lys Ile Ser Lys Gln Gln Leu Gln Thr
180     185     190
Val Lys Asp Arg Phe Gln Ala Phe Leu Asn Gly Glu Thr Gln Ile Met
195     200     205
Ala Asp Glu Ala Phe Met Asn Ala Val Gln Ser Tyr Tyr Glu Val Phe
210     215     220
Leu Lys Ser Asp Arg Val Ala Arg Met Val Gln Ser Gly Gly Cys Ser
225     230     235     240
Ala Asn Asp Ser Arg Glu Val Phe Lys Lys His Ile Glu Lys Arg Val
245     250     255
Arg Ser Leu Pro Glu Ile Asp Gly Leu Ser Lys Glu Thr Val Leu Ser
260     265     270
Ser Trp Met Ala Lys Phe Asp Ala Ile Tyr Arg Gly Glu Glu Asp Pro

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275	280	285
Arg Lys Gln Gln Ala Arg Met Thr Ala Ser Ala Ala Ser Glu Leu Ile		
290	295	300
Leu Ser Lys Glu Gln Leu Tyr Glu Met Phe Gln Asn Ile Leu Gly Ile		
305	310	315
Lys Lys Phe Glu His Gln Leu Leu Tyr Asn Ala Cys Gln Leu Asp Asn		
	325	330
Pro Asp Glu Gln Ala Ala Gln Ile Arg Arg Glu Leu Asp Gly Arg Leu		
	340	345
Gln Met Ala Asp Gln Ile Ala Arg Glu Arg Lys Phe Pro Lys Phe Val		
	355	360
Ser Lys Glu Met Glu Asn Met Tyr Ile Glu Glu Leu Lys Ser Ser Val		
	370	375
Asn Leu Leu Met Ala Asn Leu Glu Ser Met Pro Val Ser Lys Gly Gly		
	385	390
Glu Phe Lys Leu Gln Lys Leu Lys Arg Ser His Asn Ala Ser Ile Ile		
	405	410
Asp Met Gly Glu Glu Ser Glu Asn Gln Leu Ser Lys Ser Asp Val Val		
	420	425
Leu Ser Phe Ser Leu Glu Val Val Ile Met Glu Val Gln Gly Leu Lys		
	435	440
Ser Leu Ala Pro Asn Arg Ile Val Tyr Cys Thr Met Glu Val Glu Gly		
	450	455
Gly Glu Lys Leu Gln Thr Asp Gln Ala Glu Ala Ser Lys Pro Thr Trp		
	465	470
Gly Thr Gln Gly Asp Phe Ser Thr Thr His Ala Leu Pro Ala Val Lys		
	485	490
Val Lys Leu Phe Thr Glu Ser Thr Gly Val Leu Ala Leu Glu Asp Lys		
	500	505
Glu Leu Gly Arg Val Ile Leu His Pro Thr Pro Asn Ser Pro Lys Gln		
	515	520
Ser Glu Trp His Lys Met Thr Val Ser Lys Asn Cys Pro Asp Gln Asp		
	530	535
Leu Lys Ile Lys Leu Ala Val Arg Met Asp Lys Pro Gln Asn Met Lys		
	545	550
His Ser Gly Tyr Leu Trp Ala Ile Gly Lys Asn Val Trp Lys Arg Trp		
	565	570
Lys Lys Arg Phe Phe Val Leu Val Gln Val Ser Gln Tyr Thr Phe Ala		
	580	585
Met Cys Ser Tyr Arg Glu Lys Lys Ala Glu Pro Gln Glu Leu Leu Gln		
	595	600
Leu Asp Gly Tyr Thr Val Asp Tyr Thr Asp Pro Gln Pro Gly Leu Glu		
	610	615
Gly Gly Arg Ala Phe Phe Asn Ala Val Lys Glu Gly Asp Thr Val Ile		
	625	630
Phe Ala Ser Asp Asp Glu Gln Asp Arg Ile Leu Trp Val Gln Ala Met		
	645	650
Tyr Arg Ala Thr Gly Gln Ser His Lys Pro Val Pro Pro Thr Gln Val		
	660	665
Gln Lys Leu Asn Ala Lys Gly Gly Asn Val Pro Gln Leu Asp Ala Pro		
	675	680
Ile Ser Gln Phe Tyr Ala Asp Arg Ala Gln Lys His Gly Met Asp Glu		
	690	695
Phe Ile Ser Ser Asn Pro Cys Asn Phe Asp His Ala Ser Leu Phe Glu		
	705	710
Met Val Gln Arg Leu Thr Leu Asp His Arg Leu Asn Asp Ser Tyr Ser		
	725	730
Cys Leu Gly Trp Phe Ser Pro Gly Gln Val Phe Val Leu Asp Glu Tyr		
	735	



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Leu Leu Val	Ala Lys Phe Val Thr	Ile Leu Glu Gly Val	Leu Ala Lys		
	1220		1225		1230
Leu Ser Arg	Tyr Asp Glu Gly Thr	Leu Phe Ser Ser	Phe Leu Ser Phe		
	1235		1240		1245
Thr Val Lys	Ala Ala Ser Lys Tyr Val	Asp Val Pro Lys	Pro Gly Met		
	1250		1255		1260
Asp Val Ala	Asp Ala Tyr Val Thr	Phe Val Arg His	Ser Gln Asp Val		
	1265		1270		1275
Leu Arg Asp	Lys Val Asn Glu Glu Met	Tyr Ile Glu Arg	Leu Phe Asp		1280
	1285		1290		1295
Gln Trp Tyr	Asn Ser Ser Met Asn Val	Ile Cys Thr Trp	Leu Thr Asp		
	1300		1305		1310
Arg Met Asp	Leu Gln Leu His Ile Tyr	Gln Leu Lys Thr	Leu Ile Arg		
	1315		1320		1325
Val Val Lys	Lys Thr Tyr Arg Asp	Phe Arg Leu Gln	Gly Val Leu Asp		
	1330		1335		1340
Ser Thr Leu	Asn Ser Lys Thr Tyr Glu	Thr Ile Arg Asn	Arg Leu Thr		
	1345		1350		1355
Val Glu Glu	Ala Thr Ala Ser Val Ser	Glu Gly Gly Gly	Leu Gln Gly		
	1365		1370		1375
Ile Ser Met	Lys Asp Ser Asp Glu Glu	Asp Glu Asp Asp			
	1380		1385		1390

&lt;210&gt; 36

&lt;211&gt; 4828

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 36

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&lt;210&gt; 37

&lt;211&gt; 882

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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Gln Ile Lys Ser Asn Lys Asp Lys Glu Gly Lys Val Phe Tyr Ser Ile
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 385     390     395     400
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<210> 38  
 <211> 4521  
 <212> DNA  
 <213> Homo sapiens

<400> 38

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&lt;210&gt; 39

&lt;211&gt; 790

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

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Ala Lys Lys Arg Ala Leu Glu Leu Ser Gly Asn Ser Lys Asn Glu Leu
35          40          45
Asn Arg Ser Lys Arg Ser Trp Met Trp Asn Gln Phe Phe Leu Leu Glu
50          55          60
Glu Tyr Thr Gly Ser Asp Tyr Gln Tyr Val Gly Lys Leu His Ser Asp
65          70          75          80
Gln Asp Arg Gly Asp Gly Ser Leu Lys Tyr Ile Leu Ser Gly Asp Gly
85          90          95
Ala Gly Asp Leu Phe Ile Ile Asn Glu Asn Thr Gly Asp Ile Gln Ala
100          105          110
Thr Lys Arg Leu Asp Arg Glu Glu Lys Pro Val Tyr Ile Leu Arg Ala
115          120          125
Gln Ala Ile Asn Arg Arg Thr Gly Arg Pro Val Glu Pro Glu Ser Glu
130          135          140
Phe Ile Ile Lys Ile His Asp Ile Asn Asp Asn Glu Pro Ile Phe Thr
145          150          155          160
Lys Glu Val Tyr Thr Ala Thr Val Pro Glu Met Ser Asp Val Gly Thr
165          170          175
Phe Val Val Gln Val Thr Ala Thr Asp Ala Asp Asp Pro Thr Tyr Gly
180          185          190
Asn Ser Ala Lys Val Val Tyr Ser Ile Leu Gln Gly Gln Pro Tyr Phe
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 Tyr Gln Phe Lys Thr Pro Glu Ser Ser Pro Pro Gly Thr Pro Ile Gly  
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Asp Ile Gly Thr Leu Arg Asn Pro Glu Ala Ile Glu Asp Asn Lys Leu  
 675 680 685  
 Arg Arg Asp Ile Val Pro Glu Ala Leu Phe Leu Pro Arg Arg Thr Pro  
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 Thr Ala Arg Asp Asn Thr Asp Val Arg Asp Phe Ile Asn Gln Arg Leu  
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 Thr Tyr Ala Tyr Glu Gly Thr Gly Ser Val Ala Asp Ser Leu Ser Ser  
 740 745 750  
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 <212> DNA  
 <213> Homo sapiens

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 <212> PRT  
 <213> Homo sapiens

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&lt;210&gt; 43

&lt;211&gt; 1203

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 43

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Gln	Asn 450	Lys	Leu	Lys	His 455	Val	Gln	Gly	Pro	Glu	Pro 460	Ala	Lys	Glu	Val	
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His	Arg	Asp	Arg	Glu	Leu	Glu	Lys	Gln	Leu	Ala	Val	Leu	Arg	Val	Glu
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<210> 44
<211> 1925
<212> DNA
<213> Homo sapiens
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&lt;210&gt; 45

&lt;211&gt; 383

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 45

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 50          55          60
His Ile Asp Thr Trp Glu Trp Asn Asp Val Thr Leu Tyr Gly Met Leu
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Asn Thr Leu Lys Asn Arg Asn Pro Asn Leu Lys Thr Leu Leu Ser Val
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115          120          125
Thr His Gly Phe Asp Gly Leu Asp Leu Ala Trp Leu Tyr Pro Gly Arg
130          135          140
Arg Asp Lys Gln His Phe Thr Thr Leu Ile Lys Glu Met Lys Ala Glu
145          150          155          160
Phe Ile Lys Glu Ala Gln Pro Gly Lys Lys Gln Leu Leu Leu Ser Ala
165          170          175
Ala Leu Ser Ala Gly Lys Val Thr Ile Asp Ser Ser Tyr Asp Ile Ala
180          185          190
Lys Ile Ser Gln His Leu Asp Phe Ile Ser Ile Met Thr Tyr Asp Phe
195          200          205
His Gly Ala Trp Arg Gly Thr Thr Gly His His Ser Pro Leu Phe Arg
210          215          220
Gly Gln Glu Asp Ala Ser Pro Asp Arg Phe Ser Asn Thr Asp Tyr Ala
225          230          235          240
Val Gly Tyr Met Leu Arg Leu Gly Ala Pro Ala Ser Lys Leu Val Met
245          250          255
Gly Ile Pro Thr Phe Gly Arg Ser Phe Thr Leu Ala Ser Ser Glu Thr
260          265          270
Gly Val Gly Ala Pro Ile Ser Gly Pro Gly Ile Pro Gly Arg Phe Thr
275          280          285
Lys Glu Ala Gly Thr Leu Ala Tyr Tyr Glu Ile Cys Asp Phe Leu Arg

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	325	330		335
Lys Val Gln Tyr Leu Lys	Asp Arg Gln Leu Ala	Gly Ala Met Val Trp		
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Ala Leu Asp Leu Asp Asp	Phe Gln Gly Ser Phe	Cys Gly Gln Asp Leu		
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Arg Phe Pro Leu Thr Asn	Ala Ile Lys Asp Ala	Leu Ala Ala Thr		
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&lt;210&gt; 46

&lt;211&gt; 1528

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 46

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&lt;210&gt; 47

&lt;211&gt; 417

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

Met Ala Gly Pro Phe Ser Arg	Leu Leu Ser Ala Arg Pro Gly Leu Arg
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Leu Leu Ala Leu Ala Gly Ala Gly	Ser Leu Ala Ala Gly Phe Leu Leu
	20 25 30
Arg Pro Glu Pro Val Arg Ala Ala	Ser Glu Arg Arg Arg Leu Tyr Pro
	35 40 45

Pro Ser Ala Glu Tyr Pro Asp Leu Arg Lys His Asn Asn Cys Met Ala  
 50 55 60  
 Ser His Leu Thr Pro Ala Val Tyr Ala Arg Leu Cys Asp Lys Thr Thr  
 65 70 75 80  
 Pro Thr Gly Trp Thr Leu Asp Gln Cys Ile Gln Thr Gly Val Asp Asn  
 85 90 95  
 Pro Gly His Pro Phe Ile Lys Thr Val Gly Met Val Ala Gly Asp Glu  
 100 105 110  
 Glu Thr Tyr Glu Val Phe Ala Asp Leu Phe Asp Pro Val Ile Gln Glu  
 115 120 125  
 Arg His Asn Gly Tyr Asp Pro Arg Thr Met Lys His Thr Thr Asp Leu  
 130 135 140  
 Asp Ala Ser Lys Ile Arg Ser Gly Tyr Phe Asp Glu Arg Tyr Val Leu  
 145 150 155 160  
 Ser Ser Arg Val Arg Thr Gly Arg Ser Ile Arg Gly Leu Ser Leu Pro  
 165 170 175  
 Pro Ala Cys Thr Arg Ala Glu Arg Arg Glu Val Glu Arg Val Val Val  
 180 185 190  
 Asp Ala Leu Ser Gly Leu Lys Gly Asp Leu Ala Gly Arg Tyr Tyr Arg  
 195 200 205  
 Leu Ser Glu Met Thr Glu Ala Glu Gln Gln Gln Leu Ile Asp Asp His  
 210 215 220  
 Phe Leu Phe Asp Lys Pro Val Ser Pro Leu Leu Thr Ala Ala Gly Met  
 225 230 235 240  
 Ala Arg Asp Trp Pro Asp Ala Arg Gly Ile Trp His Asn Asn Glu Lys  
 245 250 255  
 Ser Phe Leu Ile Trp Val Asn Glu Glu Asp His Thr Arg Val Ile Ser  
 260 265 270  
 Met Glu Lys Gly Gly Asn Met Lys Arg Val Phe Glu Arg Phe Cys Arg  
 275 280 285  
 Gly Leu Lys Glu Val Glu Arg Leu Ile Gln Glu Arg Gly Trp Glu Phe  
 290 295 300  
 Met Trp Asn Glu Arg Leu Gly Tyr Ile Leu Thr Cys Pro Ser Asn Leu  
 305 310 315 320  
 Gly Thr Gly Leu Arg Ala Gly Val His Ile Lys Leu Pro Leu Leu Ser  
 325 330 335  
 Lys Asp Ser Arg Phe Pro Lys Ile Leu Glu Asn Leu Arg Leu Gln Lys  
 340 345 350  
 Arg Gly Thr Gly Gly Val Asp Thr Ala Ala Thr Gly Gly Val Phe Asp  
 355 360 365  
 Ile Ser Asn Leu Asp Arg Leu Gly Lys Ser Glu Val Glu Leu Val Gln  
 370 375 380  
 Leu Val Ile Asp Gly Val Asn Tyr Leu Ile Asp Cys Glu Arg Arg Leu  
 385 390 395 400  
 Glu Arg Gly Gln Asp Ile Arg Ile Pro Thr Pro Val Ile His Thr Lys  
 405 410 415  
 His

&lt;210&gt; 48

&lt;211&gt; 2365

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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tagtattttc ctgaagtgtg aaaga 2365

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&lt;210&gt; 49

&lt;211&gt; 228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 49

```

Met Ala Ser Thr Ala Ser Glu Ile Ile Ala Phe Met Val Ser Ile Ser
 1           5           10          15
Gly Trp Val Leu Val Ser Ser Thr Leu Pro Thr Asp Tyr Trp Lys Val
 20          25          30
Ser Thr Ile Asp Gly Thr Val Ile Thr Thr Ala Thr Tyr Trp Ala Asn
 35          40          45
Leu Trp Lys Ala Cys Val Thr Asp Ser Thr Gly Val Ser Asn Cys Lys
 50          55          60
Asp Phe Pro Ser Met Leu Ala Leu Asp Gly Tyr Ile Gln Ala Cys Arg
 65          70          75          80
Gly Leu Met Ile Ala Ala Val Ser Leu Gly Phe Phe Gly Ser Ile Phe
 85          90          95
Ala Leu Phe Gly Met Lys Cys Thr Lys Val Gly Gly Ser Asp Lys Ala

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<400> 50

<400> 51

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Tyr	Cys	Asn	Ser	Arg	His	Leu	Gln	Gln	Gly	Val	Arg	Lys	Ser	Lys	Arg
			20					25					30		
Pro	Val	Phe	Ser	His	Cys	Gln	Val	Pro	Glu	Thr	Gln	Lys	Thr	Asp	Thr
		35				40						45			
Arg	His	Leu	Ser	Gly	Ala	Arg	Ala	Gly	Val	Cys	Pro	Cys	Cys	His	Pro
	50	.	.			55				60					

Asp Gly Leu Leu Ala Thr Met Arg Asp Leu Leu Gln Tyr Ile Ala Cys  
 65 70 75 80  
 Phe Phe Ala Phe Phe Ser Ala Gly Phe Leu Ile Val Ala Thr Trp Thr  
 85 90 95  
 Asp Cys Trp Met Val Asn Ala Asp Asp Ser Leu Glu Val Ser Thr Lys  
 100 105 110  
 Cys Arg Gly Leu Trp Trp Glu Cys Val Thr Asn Ala Phe Asp Gly Ile  
 115 120 125  
 Arg Thr Cys Asp Glu Tyr Asp Ser Ile Leu Ala Glu His Pro Leu Lys  
 130 135 140  
 Leu Val Val Thr Arg Ala Leu Met Ile Thr Ala Asp Ile Leu Ala Gly  
 145 150 155 160  
 Phe Gly Phe Leu Thr Leu Leu Leu Gly Leu Asp Cys Val Lys Phe Leu  
 165 170 175  
 Pro Asp Glu Pro Tyr Ile Lys Val Arg Ile Cys Phe Val Ala Gly Ala  
 180 185 190  
 Thr Leu Leu Ile Ala Gly Thr Pro Gly Ile Ile Gly Ser Val Trp Tyr  
 195 200 205  
 Ala Val Asp Val Tyr Val Glu Arg Ser Thr Leu Val Leu His Asn Ile  
 210 215 220  
 Phe Leu Gly Ile Gln Tyr Lys Phe Gly Trp Ser Cys Trp Leu Gly Met  
 225 230 235 240  
 Ala Gly Ser Leu Gly Cys Phe Leu Ala Gly Ala Val Leu Thr Cys Cys  
 245 250 255  
 Leu Tyr Leu Phe Lys Asp Val Gly Pro Glu Arg Asn Tyr Pro Tyr Ser  
 260 265 270  
 Leu Arg Lys Ala Tyr Ser Ala Ala Gly Val Ser Met Ala Lys Ser Tyr  
 275 280 285  
 Ser Ala Pro Arg Thr Glu Thr Ala Lys Met Tyr Ala Val Asp Thr Arg  
 290 295 300  
 Val  
 305

&lt;210&gt; 52

&lt;211&gt; 1665

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 52

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 acggccccca cagccggatc ccctcagcct tccaggtcct caactcccgt ggacgctgaa 180  
 caatggcctc catggggcta caggtaatgg gcatcgcgct ggccgtcctg ggctggctgg 240  
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&lt;210&gt; 53

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

```

Met Ala Ser Met Gly Leu Gln Val Met Gly Ile Ala Leu Ala Val Leu
 1           5           10          15
Gly Trp Leu Ala Val Met Leu Cys Cys Ala Leu Pro Met Trp Arg Val
          20          25          30
Thr Ala Phe Ile Gly Ser Asn Ile Val Thr Ser Gln Thr Ile Trp Glu
          35          40          45
Gly Leu Trp Met Asn Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
 50          55          60
Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
 65          70          75          80
Arg Ala Leu Val Ile Ile Ser Ile Ile Val Ala Ala Leu Gly Val Leu
          85          90          95
Leu Ser Val Val Gly Gly Lys Cys Thr Asn Cys Leu Glu Asp Glu Ser
          100         105         110
Ala Lys Ala Lys Thr Met Ile Val Ala Gly Val Val Phe Leu Leu Ala
          115         120         125
Gly Leu Met Val Ile Val Pro Val Ser Trp Thr Ala His Asn Ile Ile
          130         135         140
Gln Asp Phe Tyr Asn Pro Leu Val Ala Ser Gly Gln Lys Arg Glu Met
          145         150         155         160
Gly Ala Ser Leu Tyr Val Gly Trp Ala Ala Ser Gly Leu Leu Leu Leu
          165         170         175
Gly Gly Gly Leu Leu Cys Cys Asn Cys Pro Pro Arg Thr Asp Lys Pro
          180         185         190
Tyr Ser Ala Lys Tyr Ser Ala Ala Arg Ser Ala Ala Ala Ser Asn Tyr
          195         200         205
Val

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&lt;210&gt; 54

&lt;211&gt; 3457

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(3457)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 54



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<210> 55  
 <211> 1069  
 <212> PRT  
 <213> Homo sapiens

<400> 55

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		20					25						30		
Trp	Asp	Tyr	Ala	Ser	Asp	His	Gly	Glu	Lys	Lys	Leu	Ile	Ser	Val	Asp
	35					40					45				
Thr	Glu	His	Ser	Asn	Ile	Tyr	Leu	Gln	Asn	Gly	Pro	Asp	Arg	Ile	Gly
	50				55					60					
Arg	Leu	Tyr	Lys	Lys	Ala	Leu	Tyr	Leu	Gln	Tyr	Thr	Asp	Glu	Thr	Phe
65					70				75						80
Arg	Thr	Thr	Ile	Glu	Lys	Pro	Val	Trp	Leu	Gly	Phe	Leu	Gly	Pro	Ile
			85					90						95	
Ile	Lys	Ala	Glu	Thr	Gly	Asp	Lys	Val	Tyr	Val	His	Leu	Lys	Asn	Leu
		100						105					110		
Ala	Ser	Arg	Pro	Tyr	Thr	Phe	His	Ser	His	Gly	Ile	Thr	Tyr	Tyr	Lys
	115					120						125			
Glu	His	Glu	Gly	Ala	Ile	Tyr	Pro	Asp	Asn	Thr	Thr	Asp	Phe	Gln	Arg
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Ala	Asp	Asp	Lys	Val	Tyr	Pro	Gly	Glu	Gln	Tyr	Thr	Tyr	Met	Leu	Leu
145					150				155					160	
Ala	Thr	Glu	Glu	Gln	Ser	Pro	Gly	Glu	Gly	Asp	Gly	Asn	Cys	Val	Thr
			165					170						175	
Arg	Ile	Tyr	His	Ser	His	Ile	Asp	Ala	Pro	Lys	Asp	Ile	Ala	Ser	Gly
	180						185						190		
Leu	Ile	Gly	Pro	Leu	Ile	Ile	Cys	Lys	Lys	Asp	Ser	Leu	Asp	Lys	Glu
	195					200						205			
Lys	Glu	Lys	His	Ile	Asp	Arg	Glu	Phe	Val	Val	Met	Phe	Ser	Val	Val
	210				215						220				
Asp	Glu	Asn	Phe	Ser	Trp	Tyr	Leu	Glu	Asp	Asn	Ile	Lys	Thr	Tyr	Cys
225					230					235					240
Ser	Glu	Pro	Glu	Lys	Val	Asp	Lys	Asp	Asn	Glu	Asp	Phe	Gln	Glu	Ser
			245					250						255	
Asn	Arg	Met	Tyr	Ser	Val	Asn	Gly	Tyr	Thr	Phe	Gly	Ser	Leu	Pro	Gly
		260					265						270		
Leu	Ser	Met	Cys	Ala	Glu	Asp	Arg	Val	Lys	Trp	Tyr	Leu	Phe	Gly	Met
	275					280						285			
Gly	Asn	Glu	Val	Asp	Val	His	Ala	Ala	Phe	Phe	His	Gly	Gln	Ala	Leu
	290					295					300				
Thr	Asn	Lys	Asn	Tyr	Arg	Ile	Asp	Thr	Ile	Asn	Leu	Phe	Pro	Ala	Thr
305					310					315					320
Leu	Phe	Asp	Ala	Tyr	Met	Val	Ala	Gln	Asn	Pro	Gly	Glu	Trp	Met	Leu
			325					330						335	
Ser	Cys	Gln	Asn	Leu	Asn	His	Leu	Lys	Ala	Gly	Leu	Gln	Ala	Phe	Phe
			340				345						350		
Gln	Val	Gln	Glu	Cys	Asn	Lys	Ser	Ser	Ser	Lys	Asp	Asn	Ile	Arg	Gly
	355					360						365			
Lys	His	Val	Arg	His	Tyr	Tyr	Ile	Ala	Ala	Glu	Glu	Ile	Ile	Trp	Asn
	370					375					380				
Tyr	Ala	Pro	Ser	Gly	Ile	Asp	Ile	Phe	Thr	Lys	Glu	Asn	Leu	Thr	Ala
385					390					395					400
Pro	Gly	Ser	Asp	Ser	Ala	Val	Phe	Phe	Glu	Gln	Gly	Thr	Thr	Arg	Ile

				405					410					415			
Gly	Gly	Ser	Tyr	Lys	Lys	Leu	Val	Tyr	Arg	Glu	Tyr	Thr	Asp	Ala	Ser		
			420					425					430				
Phe	Thr	Asn	Arg	Lys	Glu	Arg	Gly	Pro	Glu	Glu	Glu	His	Leu	Gly	Ile		
		435					440					445					
Leu	Gly	Pro	Val	Ile	Trp	Ala	Glu	Val	Gly	Asp	Thr	Ile	Arg	Val	Thr		
	450					455					460						
Phe	His	Asn	Lys	Gly	Ala	Tyr	Pro	Leu	Ser	Ile	Glu	Pro	Ile	Gly	Val		
465				470						475					480		
Arg	Phe	Asn	Lys	Asn	Asn	Glu	Gly	Thr	Tyr	Tyr	Ser	Pro	Asn	Tyr	Asn		
			485					490						495			
Pro	Gln	Ser	Arg	Ser	Val	Pro	Pro	Ser	Ala	Ser	His	Val	Ala	Pro	Thr		
		500					505					510					
Glu	Thr	Phe	Thr	Tyr	Glu	Trp	Thr	Val	Pro	Lys	Glu	Val	Gly	Pro	Thr		
	515						520					525					
Asn	Ala	Asp	Pro	Val	Cys	Leu	Ala	Lys	Met	Tyr	Tyr	Ser	Ala	Val	Asp		
	530					535					540						
Pro	Thr	Lys	Asp	Ile	Phe	Thr	Gly	Leu	Ile	Gly	Pro	Met	Lys	Ile	Cys		
545				550						555					560		
Lys	Lys	Gly	Ser	Leu	His	Ala	Asn	Gly	Arg	Gln	Lys	Asp	Val	Asp	Lys		
			565					570						575			
Glu	Phe	Tyr	Leu	Phe	Pro	Thr	Val	Phe	Asp	Glu	Asn	Glu	Ser	Leu	Leu		
		580						585					590				
Leu	Glu	Asp	Asn	Ile	Arg	Met	Phe	Thr	Thr	Ala	Pro	Asp	Gln	Val	Asp		
	595					600					605						
Lys	Glu	Asp	Glu	Asp	Phe	Gln	Glu	Ser	Asn	Lys	Met	His	Ser	Met	Asn		
	610					615					620						
Gly	Phe	Met	Tyr	Gly	Asn	Gln	Pro	Gly	Leu	Thr	Met	Cys	Lys	Gly	Asp		
625				630						635					640		
Ser	Val	Val	Trp	Tyr	Leu	Phe	Ser	Ala	Gly	Asn	Glu	Ala	Asp	Val	His		
			645					650						655			
Gly	Ile	Tyr	Phe	Ser	Gly	Asn	Thr	Tyr	Leu	Trp	Arg	Gly	Glu	Arg	Arg		
	660						665						670				
Asp	Thr	Ala	Asn	Leu	Phe	Pro	Gln	Thr	Ser	Leu	Thr	Leu	His	Met	Trp		
	675						680					685					
Pro	Asp	Thr	Glu	Gly	Thr	Phe	Asn	Val	Glu	Cys	Leu	Thr	Thr	Asp	His		
	690					695					700						
Tyr	Thr	Gly	Gly	Met	Lys	Gln	Lys	Tyr	Thr	Val	Asn	Gln	Cys	Arg	Arg		
705				710						715					720		
Gln	Ser	Glu	Asp	Ser	Thr	Phe	Tyr	Leu	Gly	Glu	Arg	Thr	Tyr	Tyr	Ile		
			725					730						735			
Ala	Ala	Val	Glu	Val	Glu	Trp	Asp	Tyr	Ser	Pro	Gln	Arg	Glu	Trp	Glu		
		740					745					750					
Lys	Glu	Leu	His	His	Leu	Gln	Glu	Gln	Asn	Val	Ser	Asn	Ala	Phe	Leu		
	755						760					765					
Asp	Lys	Gly	Glu	Phe	Tyr	Ile	Gly	Ser	Lys	Tyr	Lys	Lys	Val	Val	Tyr		
	770					775					780						
Arg	Gln	Tyr	Thr	Asp	Ser	Thr	Phe	Arg	Val	Pro	Val	Glu	Arg	Lys	Ala		
785				790						795					800		
Glu	Glu	Glu	His	Leu	Gly	Ile	Leu	Gly	Pro	Gln	Leu	His	Ala	Asp	Val		
			805					810						815			
Gly	Asp	Lys	Val	Lys	Ile	Ile	Phe	Lys	Asn	Met	Ala	Thr	Arg	Pro	Tyr		
		820						825					830				
Ser	Ile	His	Ala	His	Gly	Val	Gln	Thr	Glu	Ser	Ser	Thr	Val	Thr	Pro		
	835						840					845					
Thr	Leu	Pro	Gly	Glu	Thr	Leu	Thr	Tyr	Val	Trp	Lys	Ile	Pro	Glu	Arg		
	850					855					860						
Ser	Gly	Ala	Gly	Thr	Glu	Asp	Ser	Ala	Cys	Ile	Pro	Trp	Ala	Tyr	Tyr		

865		870		875		880
Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro						
	885		890		895	
Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg						
	900		905		910	
Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser						
	915		920		925	
Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys						
	930		935		940	
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala						
945	950		955		960	
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val						
	965		970		975	
Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp						
	980		985		990	
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg						
	995		1000		1005	
Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln						
	1010		1015		1020	
Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys						
1025	1030		1035		1040	
His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val						
	1045		1050		1055	
Leu Gln Asn Glu Gly Glu Tyr Pro Asp Thr Lys Ser Gly						
	1060		1065			

&lt;210&gt; 56

&lt;211&gt; 2807

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

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&lt;210&gt; 57

&lt;211&gt; 852

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 57

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Val Val Met Phe Ser Val Val Asp Glu Asn Phe Ser Trp Tyr Leu Glu
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Asp Asn Ile Lys Thr Tyr Cys Ser Glu Pro Glu Lys Val Asp Lys Asp
20          25          30
Asn Glu Asp Phe Gln Glu Ser Asn Arg Met Tyr Ser Val Asn Gly Tyr
35          40          45
Thr Phe Gly Ser Leu Pro Gly Leu Ser Met Cys Ala Glu Asp Arg Val
50          55          60
Lys Trp Tyr Leu Phe Gly Met Gly Asn Glu Val Asp Val His Ala Ala
65          70          75          80
Phe Phe His Gly Gln Ala Leu Thr Asn Lys Asn Tyr Arg Ile Asp Thr
85          90          95
Ile Asn Leu Phe Pro Ala Thr Leu Phe Asp Ala Tyr Met Val Ala Gln
100          105          110
Asn Pro Gly Glu Trp Met Leu Ser Cys Gln Asn Leu Asn His Leu Lys
115          120          125
Ala Gly Leu Gln Ala Phe Phe Gln Val Gln Glu Cys Asn Lys Ser Ser
130          135          140
Ser Lys Asp Asn Ile Arg Gly Lys His Val Arg His Tyr Tyr Ile Ala
145          150          155          160
Ala Glu Glu Ile Ile Trp Asn Tyr Ala Pro Ser Gly Ile Asp Ile Phe
165          170          175
Thr Lys Glu Asn Leu Thr Ala Pro Gly Ser Asp Ser Ala Val Phe Phe
180          185          190
Glu Gln Gly Thr Thr Arg Ile Gly Gly Ser Tyr Lys Lys Leu Val Tyr
195          200          205
Arg Glu Tyr Thr Asp Ala Ser Phe Thr Asn Arg Lys Glu Arg Gly Pro
210          215          220
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Val Ile Trp Ala Glu Val

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225		230		235		240
Gly Asp Thr Ile Arg Val Thr Phe His Asn Lys Gly Ala Tyr Pro Leu						
	245		250		255	
Ser Ile Glu Pro Ile Gly Val Arg Phe Asn Lys Asn Asn Glu Gly Thr						
	260		265		270	
Tyr Tyr Ser Pro Asn Tyr Asn Pro Gln Ser Arg Ser Val Pro Pro Ser						
	275		280		285	
Ala Ser His Val Ala Pro Thr Glu Thr Phe Thr Tyr Glu Trp Thr Val						
	290		295		300	
Pro Lys Glu Val Gly Pro Thr Asn Ala Asp Pro Val Cys Leu Ala Lys						
	305		310		315	
Met Tyr Tyr Ser Ala Val Asp Pro Thr Lys Asp Ile Phe Thr Gly Leu						
	325		330		335	
Ile Gly Pro Met Lys Ile Cys Lys Lys Gly Ser Leu His Ala Asn Gly						
	340		345		350	
Arg Gln Lys Asp Val Asp Lys Glu Phe Tyr Leu Phe Pro Thr Val Phe						
	355		360		365	
Asp Glu Asn Glu Ser Leu Leu Leu Glu Asp Asn Ile Arg Met Phe Thr						
	370		375		380	
Thr Ala Pro Asp Gln Val Asp Lys Glu Asp Glu Asp Phe Gln Glu Ser						
	385		390		395	
Asn Lys Met His Ser Met Asn Gly Phe Met Tyr Gly Asn Gln Pro Gly						
	405		410		415	
Leu Thr Met Cys Lys Gly Asp Ser Val Val Trp Tyr Leu Phe Ser Ala						
	420		425		430	
Gly Asn Glu Ala Asp Val His Gly Ile Tyr Phe Ser Gly Asn Thr Tyr						
	435		440		445	
Leu Trp Arg Gly Glu Arg Arg Asp Thr Ala Asn Leu Phe Pro Gln Thr						
	450		455		460	
Ser Leu Thr Leu His Met Trp Pro Asp Thr Glu Gly Thr Phe Asn Val						
	465		470		475	
Glu Cys Leu Thr Thr Asp His Tyr Thr Gly Gly Met Lys Gln Lys Tyr						
	485		490		495	
Thr Val Asn Gln Cys Arg Arg Gln Ser Glu Asp Ser Thr Phe Tyr Leu						
	500		505		510	
Gly Glu Arg Thr Tyr Tyr Ile Ala Val Glu Val Glu Trp Asp Tyr						
	515		520		525	
Ser Pro Gln Arg Glu Trp Glu Lys Glu Leu His His Leu Gln Glu Gln						
	530		535		540	
Asn Val Ser Asn Ala Phe Leu Asp Lys Gly Glu Phe Tyr Ile Gly Ser						
	545		550		555	
Lys Tyr Lys Lys Val Val Tyr Arg Gln Tyr Thr Asp Ser Thr Phe Arg						
	565		570		575	
Val Pro Val Glu Arg Lys Ala Glu Glu His Leu Gly Ile Leu Gly						
	580		585		590	
Pro Gln Leu His Ala Asp Val Gly Asp Lys Val Lys Ile Ile Phe Lys						
	595		600		605	
Asn Met Ala Thr Arg Pro Tyr Ser Ile His Ala His Gly Val Gln Thr						
	610		615		620	
Glu Ser Ser Thr Val Thr Pro Thr Leu Pro Gly Glu Thr Leu Thr Tyr						
	625		630		635	
Val Trp Lys Ile Pro Glu Arg Ser Gly Ala Gly Thr Glu Asp Ser Ala						
	645		650		655	
Cys Ile Pro Trp Ala Tyr Tyr Ser Thr Val Asp Gln Val Lys Asp Leu						
	660		665		670	
Tyr Ser Gly Leu Ile Gly Pro Leu Ile Val Cys Arg Arg Pro Tyr Leu						
	675		680		685	
Lys Val Phe Asn Pro Arg Arg Lys Leu Glu Phe Ala Leu Leu Phe Leu						

690		695		700
Val Phe Asp Glu Asn Glu Ser Trp Tyr Leu Asp		Asp Asn Ile Lys Thr		
705		710		715
Tyr Ser Asp His Pro Glu Lys Val Asn Lys Asp		Asp Glu Glu Phe Ile		720
		725		730
				735
Glu Ser Asn Lys Met His Ala Ile Asn Gly Arg		Met Phe Gly Asn Leu		
		740		745
				750
Gln Gly Leu Thr Met His Val Gly Asp Glu Val		Asn Trp Tyr Leu Met		
		755		760
				765
Gly Met Gly Asn Glu Ile Asp Leu His Thr Val		His Phe His Gly His		
		770		775
				780
Ser Phe Gln Tyr Lys His Arg Gly Val Tyr Ser		Ser Asp Val Phe Asp		
785		790		795
				800
Ile Phe Pro Gly Thr Tyr Gln Thr Leu Glu Met		Phe Pro Arg Thr Pro		
		805		810
				815
Gly Ile Trp Leu Leu His Cys His Val Thr Asp		His Ile His Ala Gly		
		820		825
				830
Met Glu Thr Thr Tyr Thr Val Leu Gln Asn Glu		Gly Glu Tyr Pro Asp		
		835		840
				845
Thr Lys Ser Gly				
850				

&lt;210&gt; 58

&lt;211&gt; 3321

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 58

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caccgccgaa aagtaaacaa agatgatgag gaattcatag aaagcaataa aatgcatgct 2880
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catagcttcc aatacaagca caggggagtt tatagttctg atgtctttga cattttccct 3060
ggaacatacc aaacctaga aatgtttcca agaacacctg gaatttgggtt actccactgc 3120
catgtgaccg accacattca tgctggaatg gaaaccactt acaccgttct acaaaatgaa 3180
gacaccaaat ctggctgaat gaaataaatt ggtgataagt ggaaaaaaga gaaaaaccaa 3240
tgattcataa caatgtatgt gaaagtgtaa aatagaatgt tactttggaa tgactataaa 3300
cattaaaga gactggagca t 3321

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&lt;210&gt; 59

&lt;211&gt; 1065

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 59

```

Met Lys Ile Leu Ile Leu Gly Ile Phe Leu Phe Leu Cys Ser Thr Pro
 1           5           10           15
Ala Trp Ala Lys Glu Lys His Tyr Tyr Ile Gly Ile Ile Glu Thr Thr
      20           25           30
Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
      35           40           45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
      50           55           60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
      65           70           75           80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
      85           90           95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
      100          105          110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
      115          120          125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
      130          135          140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
      145          150          155          160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
      165          170          175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
      180          185          190

```



Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu  
 195 200 205  
 Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val  
 210 215 220  
 Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys  
 225 230 235 240  
 Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser  
 245 250 255  
 Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly  
 260 265 270  
 Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met  
 275 280 285  
 Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu  
 290 295 300  
 Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr  
 305 310 315 320  
 Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu  
 325 330 335  
 Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe  
 340 345 350  
 Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly  
 355 360 365  
 Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn  
 370 375 380  
 Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala  
 385 390 395 400  
 Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile  
 405 410 415  
 Gly Gly Ser Tyr Lys Lys Leu Val Tyr Arg Glu Tyr Thr Asp Ala Ser  
 420 425 430  
 Phe Thr Asn Arg Lys Glu Arg Gly Pro Glu Glu Glu His Leu Gly Ile  
 435 440 445  
 Leu Gly Pro Val Ile Trp Ala Glu Val Gly Asp Thr Ile Arg Val Thr  
 450 455 460  
 Phe His Asn Lys Gly Ala Tyr Pro Leu Ser Ile Glu Pro Ile Gly Val  
 465 470 475 480  
 Arg Phe Asn Lys Asn Asn Glu Gly Thr Tyr Tyr Ser Pro Asn Tyr Asn  
 485 490 495  
 Pro Gln Ser Arg Ser Val Pro Pro Ser Ala Ser His Val Ala Pro Thr  
 500 505 510  
 Glu Thr Phe Thr Tyr Glu Trp Thr Val Pro Lys Glu Val Gly Pro Thr  
 515 520 525  
 Asn Ala Asp Pro Val Cys Leu Ala Lys Met Tyr Tyr Ser Ala Val Asp  
 530 535 540  
 Pro Thr Lys Asp Ile Phe Thr Gly Leu Ile Gly Pro Met Lys Ile Cys  
 545 550 555 560  
 Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys  
 565 570 575  
 Glu Phe Tyr Leu Phe Pro Thr Val Phe Asp Glu Asn Glu Ser Leu Leu  
 580 585 590  
 Leu Glu Asp Asn Ile Arg Met Phe Thr Thr Ala Pro Asp Gln Val Asp  
 595 600 605  
 Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn  
 610 615 620  
 Gly Phe Met Tyr Gly Asn Gln Pro Gly Leu Thr Met Cys Lys Gly Asp  
 625 630 635 640  
 Ser Val Val Trp Tyr Leu Phe Ser Ala Gly Asn Glu Ala Asp Val His  
 645 650 655

Gly Ile Tyr Phe Ser Gly Asn Thr Tyr Leu Trp Arg Gly Glu Arg Arg  
 660 665 670  
 Asp Thr Ala Asn Leu Phe Pro Gln Thr Ser Leu Thr Leu His Met Trp  
 675 680 685  
 Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His  
 690 695 700  
 Tyr Thr Gly Gly Met Lys Gln Lys Tyr Thr Val Asn Gln Cys Arg Arg  
 705 710 715 720  
 Gln Ser Glu Asp Ser Thr Phe Tyr Leu Gly Glu Arg Thr Tyr Tyr Ile  
 725 730 735  
 Ala Ala Val Glu Val Glu Trp Asp Tyr Ser Pro Gln Arg Glu Trp Glu  
 740 745 750  
 Lys Glu Leu His His Leu Gln Glu Gln Asn Val Ser Asn Ala Phe Leu  
 755 760 765  
 Asp Lys Gly Glu Phe Tyr Ile Gly Ser Lys Tyr Lys Lys Val Val Tyr  
 770 775 780  
 Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val Pro Val Glu Arg Lys Ala  
 785 790 795 800  
 Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val  
 805 810 815  
 Gly Asp Lys Val Lys Ile Ile Phe Lys Asn Met Ala Thr Arg Pro Tyr  
 820 825 830  
 Ser Ile His Ala His Gly Val Gln Thr Glu Ser Ser Thr Val Thr Pro  
 835 840 845  
 Thr Leu Pro Gly Glu Thr Leu Thr Tyr Val Trp Lys Ile Pro Glu Arg  
 850 855 860  
 Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr  
 865 870 875 880  
 Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro  
 885 890 895  
 Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg  
 900 905 910  
 Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser  
 915 920 925  
 Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys  
 930 935 940  
 Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala  
 945 950 955 960  
 Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val  
 965 970 975  
 Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp  
 980 985 990  
 Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg  
 995 1000 1005  
 Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln  
 1010 1015 1020  
 Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys  
 1025 1030 1035 1040  
 His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val  
 1045 1050 1055  
 Leu Gln Asn Glu Asp Thr Lys Ser Gly  
 1060 1065

&lt;210&gt; 60

&lt;211&gt; 3881

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(3881)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 60

```

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ccagcctggg cgaaagaaaa gcattattac attggaatta ttgaaacgac ttgggattat 180
gcctctgacc atggggaaaa gaaacttatt tctgttgaca cggaacattc caatatctat 240
cttcaaaatg gccagatag aattgggaga ctatataaga aggcccttta tcttcagtac 300
acagatgaaa ctttaggac aactatagaa aaaccggtct ggcttggtt tttaggccct 360
attatcaaag ctgaaactgg agataaagtt tatgtacact taaaaaacct tgcccttagg 420
ccctacacct ttcattcaca tggataaact tactataagg aacatgaggg ggccatctac 480
cctgataaca ccacagattt tcaaagagca gatgacaaag tatatccagg agagcagtat 540
acatacatgt tgcttgccac tgaagaacaa agtcctgggg aaggagatgg caattgtgtg 600
actaggattt accattccca cattgatgct ccaaaagata ttgcctcagg actcatcgga 660
cctttaataa tctgtaaaaa agattctcta gataaagaaa aagaaaaaca tattgaccga 720
gaatttgtgg tgatgttttc tgtggtggat gaaaatttca gctggtacct agaagacaac 780
attaaaacct actgctcaga accagagaaa gttgacaaag acaacgaaga cttccaggag 840
agtaacagaa tgtattctgt gaatggatac acttttggaa gtctcccagg actctccatg 900
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tgattatgta tgtctgtttt ttcaataaac aaacaaatga aaaaaaaaaa aaaaaaatgg 3840
cggccgcaag cttattancc tttagtgagg gttaatttta a 3881

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&lt;210&gt; 61

&lt;211&gt; 1090

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 61

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Met Lys Ile Leu Ile Leu Gly Ile Phe Leu Phe Leu Cys Ser Thr Pro
 1           5           10           15
Ala Trp Ala Lys Glu Lys His Tyr Tyr Ile Gly Ile Ile Glu Thr Thr
 20           25           30
Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
 35           40           45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
 50           55           60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
 65           70           75           80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
 85           90           95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
100           105           110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
115           120           125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
130           135           140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
145           150           155           160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
165           170           175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
180           185           190
Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu
195           200           205
Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
210           215           220
Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
225           230           235           240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
245           250           255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
260           265           270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
275           280           285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu

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290		295		300
Thr Asn Lys Asn Tyr Arg	Ile Asp Thr Ile Asn	Leu Phe Pro Ala Thr		
305	310	315		320
Leu Phe Asp Ala Tyr Met	Val Ala Gln Asn Pro	Gly Glu Trp Met Leu		
	325	330		335
Ser Cys Gln Asn Leu Asn	His Leu Lys Ala Gly	Leu Gln Ala Phe Phe		
	340	345		350
Gln Val Gln Glu Cys Asn	Lys Ser Ser Ser Lys	Asp Asn Ile Arg Gly		
	355	360		365
Lys His Val Arg His Tyr	Tyr Ile Ala Ala Glu	Glu Ile Ile Trp Asn		
	370	375		380
Tyr Ala Pro Ser Gly Ile	Asp Ile Phe Thr Lys	Glu Asn Leu Thr Ala		
385	390	395		400
Pro Gly Ser Asp Ser Ala	Val Phe Phe Glu Gln	Gly Thr Thr Arg Ile		
	405	410		415
Gly Gly Ser Tyr Lys Lys	Leu Val Tyr Arg Glu	Tyr Thr Asp Ala Ser		
	420	425		430
Phe Thr Asn Arg Lys Glu	Arg Gly Pro Glu Glu	Glu His Leu Gly Ile		
	435	440		445
Leu Gly Pro Val Ile Trp	Ala Glu Val Gly Asp	Thr Ile Arg Val Thr		
	450	455		460
Phe His Asn Lys Gly Ala	Tyr Pro Leu Ser Ile	Glu Pro Ile Gly Val		
465	470	475		480
Arg Phe Asn Lys Asn Asn	Glu Gly Thr Tyr Tyr	Ser Pro Asn Tyr Asn		
	485	490		495
Pro Gln Ser Arg Ser Val	Pro Pro Ser Ala Ser	His Val Ala Pro Thr		
	500	505		510
Glu Thr Phe Thr Tyr Glu	Trp Thr Val Pro Lys	Glu Val Gly Pro Thr		
	515	520		525
Asn Ala Asp Pro Val Cys	Leu Ala Lys Met Tyr	Tyr Ser Ala Val Asp		
	530	535		540
Pro Thr Lys Asp Ile Phe	Thr Gly Leu Ile Gly	Pro Met Lys Ile Cys		
545	550	555		560
Lys Lys Gly Ser Leu His	Ala Asn Gly Arg Gln	Lys Asp Val Asp Lys		
	565	570		575
Glu Phe Tyr Leu Phe Pro	Thr Val Phe Asp Glu	Asn Glu Ser Leu Leu		
	580	585		590
Leu Glu Asp Asn Ile Arg	Met Phe Thr Thr Ala	Pro Asp Gln Val Asp		
	595	600		605
Lys Glu Asp Glu Asp Phe	Gln Glu Ser Asn Lys	Met His Ser Met Asn		
	610	615		620
Gly Phe Met Tyr Gly Asn	Gln Pro Gly Leu Thr	Met Cys Lys Gly Asp		
625	630	635		640
Ser Val Val Trp Tyr Leu	Phe Ser Ala Gly Asn	Glu Ala Asp Val His		
	645	650		655
Gly Ile Tyr Phe Ser Gly	Asn Thr Tyr Leu Trp	Arg Gly Glu Arg Arg		
	660	665		670
Asp Thr Ala Asn Leu Phe	Pro Gln Thr Ser Leu	Thr Leu His Met Trp		
	675	680		685
Pro Asp Thr Glu Gly Thr	Phe Asn Val Glu Cys	Leu Thr Thr Asp His		
	690	695		700
Tyr Thr Gly Gly Met Lys	Gln Lys Tyr Thr Val	Asn Gln Cys Arg Arg		
705	710	715		720
Gln Ser Glu Asp Ser Thr	Phe Tyr Leu Gly Glu	Arg Thr Tyr Tyr Ile		
	725	730		735
Ala Ala Val Glu Val Glu	Trp Asp Tyr Ser Pro	Gln Arg Glu Trp Glu		
	740	745		750
Lys Glu Leu His His Leu	Gln Glu Gln Asn Val	Ser Asn Ala Phe Leu		

755	760	765
Asp Lys Gly Glu Phe Tyr Ile Gly Ser Lys Tyr Lys Lys Val Val Tyr		
770	775	780
Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val Pro Val Glu Arg Lys Ala		
785	790	795
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val		
805	810	815
Gly Asp Lys Val Lys Ile Ile Phe Lys Asn Met Ala Thr Arg Pro Tyr		
820	825	830
Ser Ile His Ala His Gly Val Gln Thr Glu Ser Ser Thr Val Thr Pro		
835	840	845
Thr Leu Pro Gly Glu Thr Leu Thr Tyr Val Trp Lys Ile Pro Glu Arg		
850	855	860
Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr		
865	870	875
Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro		
885	890	895
Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg		
900	905	910
Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser		
915	920	925
Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys		
930	935	940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala		
945	950	955
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val		
965	970	975
Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp		
980	985	990
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg		
995	1000	1005
Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln		
1010	1015	1020
Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys		
1025	1030	1035
His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val		
1045	1050	1055
Leu Gln Asn Glu Ala Ser Ser Glu Thr His Arg Arg Ile Trp Asn Val		
1060	1065	1070
Ile Tyr Pro Ile Thr Val Ser Val Ile Ile Leu Phe Gln Ile Ser Thr		
1075	1080	1085
Lys Glu		
1090		

&lt;210&gt; 62

&lt;211&gt; 969

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

```

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cctcccgcg cgccaccatg cccaacttct ctggcaactg gaaaatcatc cgatcggaaa 180
acttcgagga attgctcaaa gtgctggggg tgaatgtgat gctgaggaag attgctgtgg 240
ctgcagcgtc caagccagca gtggagatca aacaggaggg agacactttc tacatcaaaa 300
cctccaccac cgtgcgcacc acagagatta acttcaaggt tggggaggag tttgaggagc 360
agactgtgga tgggaggccc tgtaagagcc tggtgaaatg ggagagttag aataaaatgg 420

```

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acgtccgaga gtgagtggcc acaggtagaa ccgcggccga agcccaccac tggccatgct 600
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gggtctctct aaaggggact tgagggcctg agcaggaaag actggccctc tagcttctac 900
cctttgtccc tgtagcctat acagtttaga atatttattt gttaatttta ttaaaatgct 960
ttaaaaaaa

```

&lt;210&gt; 63

&lt;211&gt; 138

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 63

```

Met Pro Asn Phe Ser Gly Asn Trp Lys Ile Ile Arg Ser Glu Asn Phe
1          5          10          15
Glu Glu Leu Leu Lys Val Leu Gly Val Asn Val Met Leu Arg Lys Ile
20          25          30
Ala Val Ala Ala Ala Ser Lys Pro Ala Val Glu Ile Lys Gln Glu Gly
35          40          45
Asp Thr Phe Tyr Ile Lys Thr Ser Thr Thr Val Arg Thr Thr Glu Ile
50          55          60
Asn Phe Lys Val Gly Glu Glu Phe Glu Glu Gln Thr Val Asp Gly Arg
65          70          75          80
Pro Cys Lys Ser Leu Val Lys Trp Glu Ser Glu Asn Lys Met Val Cys
85          90          95
Glu Gln Lys Leu Leu Lys Gly Glu Gly Pro Lys Thr Ser Trp Thr Arg
100          105          110
Glu Leu Thr Asn Asp Gly Glu Leu Ile Leu Thr Met Thr Ala Asp Asp
115          120          125
Val Val Cys Thr Arg Val Tyr Val Arg Glu
130          135

```

&lt;210&gt; 64

&lt;211&gt; 927

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

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927

&lt;210&gt; 65

&lt;211&gt; 114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

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Met Ser Ala Leu Ser Leu Leu Ile Leu Gly Leu Leu Thr Ala Val Pro
 1           5           10           15
Pro Ala Ser Cys Gln Gln Gly Leu Gly Asn Leu Gln Pro Trp Met Gln
      20           25           30
Gly Leu Ile Ala Val Ala Val Phe Leu Val Leu Val Ala Ile Ala Phe
      35           40           45
Ala Val Asn His Phe Trp Cys Gln Glu Glu Pro Glu Pro Ala His Met
      50           55           60
Ile Leu Thr Val Gly Asn Lys Ala Asp Gly Val Leu Val Gly Thr Asp
      65           70           75           80
Gly Arg Tyr Ser Ser Met Ala Ala Ser Phe Arg Ser Ser Glu His Glu
      85           90           95
Asn Ala Tyr Glu Asn Val Pro Glu Glu Glu Gly Lys Val Arg Ser Thr
      100          105          110
Pro Met

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&lt;210&gt; 66

&lt;211&gt; 3641

&lt;212&gt; DNA .

&lt;213&gt; Homo sapiens

&lt;400&gt; 66

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aacagcagtt gaacatggac gaaggaattc ctcatcttga agagagacag ttactggaac 180
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tgcaaaagaa aaacctacca attaaaaaaa aaaaaaaaaa a 3641

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&lt;210&gt; 67

&lt;211&gt; 482

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 67

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Met Asp Glu Gly Ile Pro His Leu Gln Glu Arg Gln Leu Leu Glu His
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Arg Asp Phe Ile Gly Leu Asp Tyr Ser Ser Leu Tyr Met Cys Lys Pro
20        25        30
Lys Arg Ser Met Lys Arg Asp Asp Thr Lys Asp Thr Tyr Lys Leu Pro
35        40        45
His Arg Leu Ile Glu Lys Lys Arg Arg Asp Arg Ile Asn Glu Cys Ile
50        55        60
Ala Gln Leu Lys Asp Leu Leu Pro Glu His Leu Lys Leu Thr Thr Leu
65        70        75        80
Gly His Leu Glu Lys Ala Val Val Leu Glu Leu Thr Leu Lys His Leu
85        90        95
Lys Ala Leu Thr Ala Leu Thr Glu Gln Gln His Gln Lys Ile Ile Ala
100       105       110
Leu Gln Asn Gly Glu Arg Ser Leu Lys Ser Pro Ile Gln Ser Asp Leu
115       120       125

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Asp Ala Phe His Ser Gly Phe Gln Thr Cys Ala Lys Glu Val Leu Gln  
 130 135 140  
 Tyr Leu Ser Arg Phe Glu Ser Trp Thr Pro Arg Glu Pro Arg Cys Val  
 145 150 155 160  
 Gln Leu Ile Asn His Leu His Ala Val Ala Thr Gln Phe Leu Pro Thr  
 165 170 175  
 Pro Gln Leu Leu Thr Gln Gln Val Pro Leu Ser Lys Gly Thr Gly Ala  
 180 185 190  
 Pro Ser Ala Ala Gly Ser Ala Ala Ala Pro Cys Leu Glu Arg Ala Gly  
 195 200 205  
 Gln Lys Leu Glu Pro Leu Ala Tyr Cys Val Pro Val Ile Gln Arg Thr  
 210 215 220  
 Gln Pro Ser Ala Glu Leu Ala Ala Glu Asn Asp Thr Asp Thr Asp Ser  
 225 230 235 240  
 Gly Tyr Gly Gly Glu Ala Glu Ala Arg Pro Asp Arg Glu Lys Gly Lys  
 245 250 255  
 Gly Ala Gly Ala Ser Arg Val Thr Ile Lys Gln Glu Pro Pro Gly Glu  
 260 265 270  
 Asp Ser Pro Ala Pro Lys Arg Met Lys Leu Asp Ser Arg Gly Gly Gly  
 275 280 285  
 Ser Gly Gly Gly Pro Gly Gly Gly Ala Ala Ala Ala Ala Ala Leu  
 290 295 300  
 Leu Gly Pro Asp Pro Ala Ala Ala Ala Ala Leu Leu Arg Pro Asp Ala  
 305 310 315 320  
 Ala Leu Leu Ser Ser Leu Val Ala Phe Gly Gly Gly Gly Ala Pro  
 325 330 335  
 Phe Pro Gln Pro Ala Ala Ala Ala Ala Pro Phe Cys Leu Pro Phe Cys  
 340 345 350  
 Phe Leu Ser Pro Ser Ala Ala Ala Ala Tyr Val Gln Pro Phe Leu Asp  
 355 360 365  
 Lys Ser Gly Leu Glu Lys Tyr Leu Tyr Pro Ala Ala Ala Ala Pro  
 370 375 380  
 Phe Pro Leu Leu Tyr Pro Gly Ile Pro Ala Pro Ala Ala Ala Ala  
 385 390 395 400  
 Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Phe Pro Cys Leu Ser  
 405 410 415  
 Ser Val Leu Ser Pro Pro Pro Glu Lys Ala Gly Ala Ala Ala Thr  
 420 425 430  
 Leu Leu Pro His Glu Val Ala Pro Leu Gly Ala Pro His Pro Gln His  
 435 440 445  
 Pro His Gly Arg Thr His Leu Pro Phe Ala Gly Pro Arg Glu Pro Gly  
 450 455 460  
 Asn Pro Glu Ser Ser Ala Gln Glu Asp Pro Ser Gln Pro Gly Lys Glu  
 465 470 475 480  
 Ala Pro

&lt;210&gt; 68

&lt;211&gt; 3624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 68

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<210> 69  
 <211> 341  
 <212> PRT  
 <213> Homo sapiens

<400> 69

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      20           25           30
Ser Val Ala Gly Gln Val Cys Leu Ile Thr Gly Ala Gly Ser Gly Leu
      35           40           45
Gly Arg Leu Phe Ala Leu Glu Phe Ala Arg Arg Arg Ala Leu Leu Val
      50           55           60
Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val
      65           70           75           80
Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln
      85           90           95
Ala Gly Asn Gly Glu Glu Glu Ile Leu Pro His Cys Asn Leu Gln Val
      100          105          110
Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr
      115          120          125
Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn
      130          135          140
Asn Ala Gly Val Val Ser Gly His His Leu Leu Glu Cys Pro Asp Glu
      145          150          155          160
Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr
      165          170          175
Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile
      180          185          190
Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu
      195          200          205
Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu
      210          215          220
Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu
      225          230          235          240
Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg Ile
      245          250          255
Arg Lys Glu Ile Glu Pro Phe Leu Pro Pro Leu Lys Pro Asp Tyr Cys
      260          265          270
Val Lys Gln Ala Met Lys Ala Ile Leu Thr Asp Gln Pro Met Ile Cys
      275          280          285
Thr Pro Arg Leu Met Tyr Ile Val Thr Phe Met Lys Ser Ile Leu Pro
      290          295          300
Phe Glu Ala Val Val Cys Met Tyr Arg Phe Leu Gly Ala Asp Lys Cys
      305          310          315          320
Met Tyr Pro Phe Ile Ala Gln Arg Lys Gln Ala Thr Asn Asn Asn Glu
      325          330          335
Ala Lys Asn Gly Ile
      340

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<210> 70  
 <211> 1428  
 <212> DNA  
 <213> Homo sapiens

<400> 70

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&lt;210&gt; 71

&lt;211&gt; 289

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 71

```

Met Thr Gly Val Phe Asp Arg Arg Val Pro Ser Ile Arg Ser Gly Asp
 1           5           10          15
Phe Gln Ala Pro Phe Gln Thr Ser Ala Ala Met His His Pro Ser Gln
 20          25          30
Glu Ser Pro Thr Leu Pro Glu Ser Ser Ala Thr Asp Ser Asp Tyr Tyr
 35          40          45
Ser Pro Thr Gly Gly Ala Pro His Gly Tyr Cys Ser Pro Thr Ser Ala
 50          55          60
Ser Tyr Gly Lys Ala Leu Asn Pro Tyr Gln Tyr Gln Tyr His Gly Val
 65          70          75          80
Asn Gly Ser Ala Gly Ser Tyr Pro Ala Lys Ala Tyr Ala Asp Tyr Ser
 85          90          95
Tyr Ala Ser Ser Tyr His Gln Tyr Gly Gly Ala Tyr Asn Arg Val Pro
100          105          110
Ser Ala Thr Asn Gln Pro Glu Lys Glu Val Thr Glu Pro Glu Val Arg
115          120          125
Met Val Asn Gly Lys Pro Lys Lys Val Arg Lys Pro Arg Thr Ile Tyr
130          135          140
Ser Ser Phe Gln Leu Ala Ala Leu Gln Arg Arg Phe Gln Lys Thr Gln
145          150          155          160
Tyr Leu Ala Leu Pro Glu Arg Ala Glu Leu Ala Ala Ser Leu Gly Leu
165          170          175
Thr Gln Thr Gln Val Lys Ile Trp Phe Gln Asn Lys Arg Ser Lys Ile
180          185          190
Lys Lys Ile Met Lys Asn Gly Glu Met Pro Pro Glu His Ser Pro Ser
195          200          205
Ser Ser Asp Pro Met Ala Cys Asn Ser Pro Gln Ser Pro Ala Val Trp

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210		215		220
Glu Pro Gln Gly Ser Ser Arg Ser Leu Ser His		His Pro His Ala His		
225		230		235
Pro Pro Thr Ser Asn Gln Ser Pro Ala Ser Ser Tyr Leu Glu Asn Ser				240
		245		250
Ala Ser Trp Tyr Thr Ser Ala Ala Ser Ser Ile Asn Ser His Leu Pro				255
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Pro Pro Gly Ser Leu Gln His Pro Leu Ala Leu Ala Ser Gly Thr Leu				270
		275		280
				285
Tyr				

<210> 72  
 <211> 2036  
 <212> DNA  
 <213> Homo sapiens

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<210> 73  
 <211> 434  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 73

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 Met His Gly Thr Thr Gly Phe Tyr Gln Gly Gly Asn Gly Leu Gly Asn  
 35 40 45  
 Ala Ala Gly Phe Gly Ser Val His Gln Asp Tyr Pro Ser Tyr Pro Gly  
 50 55 60  
 Phe Pro Gln Ser Gln Tyr Pro Gln Tyr Tyr Gly Ser Ser Tyr Asn Pro  
 65 70 75 80  
 Pro Tyr Val Pro Ala Ser Ser Ile Cys Pro Ser Pro Leu Ser Thr Ser  
 85 90 95  
 Thr Tyr Val Leu Gln Glu Ala Ser His Asn Val Pro Asn Gln Ser Ser  
 100 105 110  
 Glu Ser Leu Ala Gly Glu Tyr Asn Thr His Asn Gly Pro Ser Thr Pro  
 115 120 125  
 Ala Lys Glu Gly Asp Thr Asp Arg Pro His Arg Ala Ser Asp Gly Lys  
 130 135 140  
 Leu Arg Gly Arg Ser Lys Arg Ser Ser Asp Pro Ser Pro Ala Gly Asp  
 145 150 155 160  
 Asn Glu Ile Glu Arg Val Phe Val Trp Asp Leu Asp Glu Thr Ile Ile  
 165 170 175  
 Ile Phe His Ser Leu Leu Thr Gly Thr Phe Ala Ser Arg Tyr Gly Lys  
 180 185 190  
 Asp Thr Thr Thr Ser Val Arg Ile Gly Leu Met Met Glu Glu Met Ile  
 195 200 205  
 Phe Asn Leu Ala Asp Thr His Leu Phe Phe Asn Asp Leu Glu Asp Cys  
 210 215 220  
 Asp Gln Ile His Val Asp Asp Val Ser Ser Asp Asp Asn Gly Gln Asp  
 225 230 235 240  
 Leu Ser Thr Tyr Asn Phe Ser Ala Asp Gly Phe His Ser Ser Ala Pro  
 245 250 255  
 Gly Ala Asn Leu Cys Leu Gly Ser Gly Val His Gly Gly Val Asp Trp  
 260 265 270  
 Met Arg Lys Leu Ala Phe Arg Tyr Arg Arg Val Lys Glu Met Tyr Asn  
 275 280 285  
 Thr Tyr Lys Asn Asn Val Gly Gly Leu Ile Gly Thr Pro Lys Arg Glu  
 290 295 300  
 Thr Trp Leu Gln Leu Arg Ala Glu Leu Glu Ala Leu Thr Asp Leu Trp  
 305 310 315 320  
 Leu Thr His Ser Leu Lys Ala Leu Asn Leu Ile Asn Ser Arg Pro Asn  
 325 330 335  
 Cys Val Asn Val Leu Val Thr Thr Thr Gln Leu Ile Pro Ala Leu Ala  
 340 345 350  
 Lys Val Leu Leu Tyr Gly Leu Gly Ser Val Phe Pro Ile Glu Asn Ile  
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 Tyr Ser Ala Thr Lys Thr Gly Lys Glu Ser Cys Phe Glu Arg Ile Met  
 370 375 380  
 Gln Arg Phe Gly Arg Lys Ala Val Tyr Val Val Ile Gly Asp Gly Val  
 385 390 395 400  
 Glu Glu Glu Gln Gly Ala Lys Lys His Asn Met Pro Phe Trp Arg Ile  
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 Tyr Leu

<210> 74  
 <211> 1907  
 <212> DNA  
 <213> Homo sapiens

<400> 74

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<210> 75  
 <211> 371  
 <212> PRT  
 <213> Homo sapiens

<400> 75

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 20          25          30
Ala Thr Phe Gly Ala Asp Asp Leu Val Leu Thr Leu Ser Asn Pro Gln
 35          40          45
Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly Glu Gln Pro
 50          55          60
Gln Phe Trp Ser Lys Thr Gln Val Leu Asp Trp Ile Ser Tyr Gln Val
 65          70          75          80
Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser Arg Cys Asp

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85

				85					90					95		
Met	Asp	Gly	Ala	Thr	Leu	Cys	Asn	Cys	Ala	Leu	Glu	Glu	Leu	Arg	Leu	
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		115					120						125			
Thr	Ser	Ser	Ser	Ser	Asp	Glu	Leu	Ser	Trp	Ile	Ile	Glu	Leu	Leu	Glu	
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Lys	Asp	Gly	Met	Ala	Phe	Gln	Glu	Ala	Leu	Asp	Pro	Gly	Pro	Phe	Asp	
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Gln	Gly	Ser	Pro	Phe	Ala	Gln	Glu	Leu	Leu	Asp	Asp	Gly	Gln	Gln	Ala	
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Ser	Pro	Tyr	His	Pro	Gly	Ser	Cys	Gly	Ala	Gly	Ala	Pro	Ser	Pro	Gly	
		180						185					190			
Ser	Ser	Asp	Val	Ser	Thr	Ala	Gly	Thr	Gly	Ala	Ser	Arg	Ser	Ser	His	
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Ser	Ser	Asp	Ser	Gly	Gly	Ser	Asp	Val	Asp	Leu	Asp	Pro	Thr	Asp	Gly	
		210				215					220					
Lys	Leu	Phe	Pro	Ser	Asp	Gly	Phe	Arg	Asp	Cys	Lys	Lys	Gly	Asp	Pro	
		225			230					235					240	
Lys	His	Gly	Lys	Arg	Lys	Arg	Gly	Arg	Pro	Arg	Lys	Leu	Ser	Lys	Glu	
				245					250					255		
Tyr	Trp	Asp	Cys	Leu	Glu	Gly	Lys	Lys	Ser	Lys	His	Ala	Pro	Arg	Gly	
		260					265						270			
Thr	His	Leu	Trp	Glu	Phe	Ile	Arg	Asp	Ile	Leu	Ile	His	Pro	Glu	Leu	
		275					280					285				
Asn	Glu	Gly	Leu	Met	Lys	Trp	Glu	Asn	Arg	His	Glu	Gly	Val	Phe	Lys	
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Phe	Leu	Arg	Ser	Glu	Ala	Val	Ala	Gln	Leu	Trp	Gly	Gln	Lys	Lys	Lys	
		305			310					315					320	
Asn	Ser	Asn	Met	Thr	Tyr	Glu	Lys	Leu	Ser	Arg	Ala	Met	Arg	Tyr	Tyr	
			325					330					335			
Tyr	Lys	Arg	Glu	Ile	Leu	Glu	Arg	Val	Asp	Gly	Arg	Arg	Leu	Val	Tyr	
		340					345					350				
Lys	Phe	Gly	Lys	Asn	Ser	Ser	Gly	Trp	Lys	Glu	Glu	Glu	Val	Leu	Gln	
		355					360					365				
Ser	Arg	Asn														
		370														

&lt;210&gt; 76

&lt;211&gt; 3951

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(3951)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 76

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 <211> 718  
 <212> PRT  
 <213> Homo sapiens

<400> 77

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Asp	Gln	Val	Phe	Pro	Asp	Leu	Gln	Ser	Leu	Glu	Lys	His	Met	Leu	Ser
			85						90					95	
His	Thr	Glu	Glu	Arg	Glu	Tyr	Lys	Cys	Asp	Gln	Cys	Pro	Lys	Ala	Phe
			100					105					110		
Asn	Trp	Lys	Ser	Asn	Leu	Ile	Arg	His	Gln	Met	Ser	His	Asp	Ser	Gly
	115						120					125			
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Asn	Leu	Gln	Arg	His	Ile	Arg	Ser	Gln	His	Val	Gly	Ala	Arg	Ala	His
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Gln	His	Lys	His	Ile	His	Ser	Ser	Val	Lys	Pro	Phe	Ile	Ser	Phe	Ser
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Gln	Ser	Met	Tyr	Pro	Phe	Pro	Asp	Arg	Asp	Leu	Arg	Ser	Leu	Pro	Leu
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Arg	Pro	Ser	Pro	Gly	Phe	Leu	Phe	His	Pro	Gln	Met	Ser	Ala	Ile	Glu
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<212> DNA
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&lt;211&gt; 1051

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&lt;213&gt; Homo sapiens

&lt;400&gt; 79

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Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
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Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
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<210> 81

<211> 727

<212> PRT

<213> Homo sapiens

<400> 81

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Glu	Glu	Arg	Gln	Tyr	Arg	Cys	Glu	Asp	Cys	Asp	Gln	Leu	Phe	Glu	Ser
			20					25					30		
Lys	Ala	Glu	Leu	Ala	Asp	His	Gln	Lys	Phe	Pro	Cys	Ser	Thr	Pro	His
	35						40					45			
Ser	Ala	Phe	Ser	Met	Val	Glu	Glu	Asp	Phe	Gln	Gln	Lys	Leu	Glu	Ser
	50					55					60				
Glu	Asn	Asp	Leu	Gln	Glu	Ile	His	Thr	Ile	Gln	Glu	Cys	Lys	Glu	Cys
65					70				75					80	
Asp	Gln	Val	Phe	Leu	Asp	Leu	Gln	Ser	Leu	Glu	Lys	His	Met	Leu	Ser
			85						90					95	
His	Thr	Glu	Glu	Arg	Glu	Tyr	Lys	Cys	Asp	Gln	Cys	Pro	Lys	Ala	Phe
		100						105					110		
Asn	Trp	Lys	Ser	Asn	Leu	Ile	Arg	His	Gln	Met	Ser	His	Asp	Ser	Gly
	115						120					125			
Lys	His	Tyr	Glu	Cys	Glu	Asn	Cys	Ala	Lys	Val	Phe	Thr	Asp	Pro	Ser
	130					135					140				
Asn	Leu	Gln	Arg	His	Ile	Arg	Ser	Gln	His	Val	Gly	Ala	Arg	Ala	His
145					150					155				160	
Ala	Cys	Pro	Glu	Cys	Gly	Lys	Thr	Phe	Ala	Thr	Ser	Ser	Gly	Leu	Lys
			165						170					175	
Gln	His	Lys	His	Ile	His	Ser	Ser	Val	Lys	Pro	Phe	Ile	Ser	Phe	Ser
		180						185					190		
Gln	Ser	Met	Tyr	Pro	Phe	Pro	Asp	Arg	Asp	Leu	Arg	Ser	Leu	Pro	Leu
		195					200					205			
Lys	Met	Glu	Pro	Gln	Ser	Pro	Gly	Glu	Val	Lys	Lys	Leu	Gln	Lys	Gly
	210					215					220				
Ser	Ser	Glu	Ser	Pro	Phe	Asp	Leu	Thr	Thr	Lys	Arg	Lys	Asp	Glu	Lys
225					230					235				240	
Pro	Leu	Thr	Pro	Val	Pro	Ser	Lys	Pro	Pro	Val	Thr	Pro	Ala	Thr	Ser
			245							250				255	
Gln	Asp	Gln	Pro	Leu	Asp	Leu	Ser	Met	Gly	Ser	Arg	Ser	Arg	Ala	Ser
		260						265					270		
Gly	Thr	Lys	Leu	Thr	Glu	Pro	Arg	Lys	Asn	His	Val	Phe	Gly	Gly	Lys
		275					280					285			
Lys	Gly	Ser	Asn	Val	Glu	Ser	Arg	Pro	Ala	Ser	Asp	Gly	Ser	Leu	Gln
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His	Ala	Arg	Pro	Thr	Pro	Phe	Phe	Met	Asp	Pro	Ile	Tyr	Arg	Val	Glu
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Lys	Arg	Lys	Leu	Thr	Asp	Pro	Leu	Glu	Ala	Leu	Lys	Glu	Lys	Tyr	Leu
			325						330					335	
Arg	Pro	Ser	Pro	Gly	Phe	Leu	Phe	His	Pro	Gln	Phe	Gln	Leu	Pro	Asp
			340					345					350		
Gln	Arg	Thr	Trp	Met	Ser	Ala	Ile	Glu	Asn	Met	Ala	Glu	Lys	Leu	Glu

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Ser Phe Ser Ala Leu Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val
  370              375              380
Pro Ser Met Phe Asn Phe Arg Ala Pro Pro Asn Ala Leu Pro Glu Asn
 385              390              395              400
Leu Leu Arg Lys Gly Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys
      405              410              415
Ile Phe Pro Arg Ser Ala Asn Leu Thr Arg His Leu Arg Thr His Thr
      420              425              430
Gly Glu Gln Pro Tyr Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile
      435              440              445
Ser Ser Asn Leu Gln Arg His Val Arg Asn Ile His Asn Lys Glu Lys
  450              455              460
Pro Phe Lys Cys His Leu Cys Tyr Arg Cys Phe Gly Gln Gln Thr Asn
 465              470              475              480
Leu Asp Arg His Leu Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr
      485              490              495
Ala Thr Ser Ser Pro His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu
      500              505              510
Asp Asp Lys Glu Asp Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly
      515              520              525
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  530              535              540
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Ser Asp Leu Leu Asp Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp
      565              570              575
Glu Glu Asp Glu Asp Tyr Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro
      580              585              590
Val Thr Ser Asn Leu His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu
      595              600              605
Thr Ser Ala Leu Glu Met Ser Cys Lys Thr Ser Pro Val Arg Tyr Lys
  610              615              620
Glu Glu Glu Tyr Lys Ser Gly Leu Ser Ala Leu Asp His Ile Arg His
 625              630              635              640
Phe Thr Asp Ser Leu Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser
      645              650              655
Glu Ala Glu Leu Ser Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu
      660              665              670
Lys Gln Pro Leu His Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met
      675              680              685
Leu Ser Leu Ser Asp Lys Glu Ser Leu His Ser Thr Ser His Ser Ser
  690              695              700
Ser Asn Val Trp His Ser Met Ala Arg Ala Ala Glu Ser Ser Ala
 705              710              715              720
Ile Gln Ser Ile Ser His Val
      725

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&lt;210&gt; 82

&lt;211&gt; 4923

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(4923)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 82

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ttn
4923

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&lt;210&gt; 83

&lt;211&gt; 1042

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 83

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Glu Glu Arg Gln Tyr Arg Cys Glu Asp Cys Asp Gln Leu Phe Glu Ser
20           25           30
Lys Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro His
35           40           45
Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
50           55           60
Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
65           70           75           80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
85           90           95
His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
100          105          110
Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
115          120          125
Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser
130          135          140
Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His
145          150          155          160
Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
165          170          175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
180          185          190

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Cys	His	Lys	Ser	Tyr	Thr	Gln	Phe	Ser	Asn	Leu	Cys	Arg	His	Lys	Arg
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Met	His	Ala	Asp	Cys	Arg	Thr	Gln	Ile	Lys	Cys	Lys	Asp	Cys	Gly	Gln
		210					215					220			
Met	Phe	Ser	Thr	Thr	Ser	Ser	Leu	Asn	Lys	His	Arg	Arg	Phe	Cys	Glu
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Gly	Lys	Asn	His	Phe	Ala	Ala	Gly	Gly	Phe	Phe	Gly	Gln	Gly	Ile	Ser
Leu	Pro	Gly	Thr	Pro	Ala	Met	Asp	Lys	Thr	Ser	Met	Val	Asn	Met	Ser
His	Ala	Asn	Pro	Gly	Leu	Ala	Asp	Tyr	Phe	Gly	Ala	Asn	Arg	His	Pro
Ala	Gly	Leu	Thr	Phe	Pro	Thr	Ala	Pro	Gly	Phe	Ser	Phe	Ser	Phe	Pro
Gly	Leu	Phe	Pro	Ser	Gly	Leu	Tyr	His	Arg	Pro	Pro	Leu	Ile	Pro	Ala
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Ser	Ser	Pro	Val	Lys	Gly	Leu	Ser	Ser	Thr	Glu	Gln	Thr	Asn	Lys	Ser
Gln	Ser	Pro	Leu	Met	Thr	His	Pro	Gln	Ile	Leu	Pro	Ala	Thr	Gln	Asp
Ile	Leu	Lys	Ala	Leu	Ser	Lys	His	Pro	Ser	Val	Gly	Asp	Asn	Lys	Pro
Val	Glu	Leu	Gln	Pro	Glu	Arg	Ser	Ser	Glu	Glu	Arg	Pro	Phe	Glu	Lys
Ile	Ser	Asp	Gln	Ser	Glu	Ser	Ser	Asp	Leu	Asp	Asp	Val	Ser	Thr	Pro
385															400
Ser	Gly	Ser	Asp	Leu	Glu	Thr	Thr	Ser	Gly	Ser	Asp	Leu	Glu	Ser	Asp
Ile	Glu	Ser	Asp	Lys	Glu	Lys	Phe	Lys	Glu	Asn	Gly	Lys	Met	Phe	Lys
Asp	Lys	Val	Ser	Pro	Leu	Gln	Asn	Leu	Ala	Ser	Ile	Asn	Asn	Lys	Lys

Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln Met  
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 Ser Ala Ile Glu Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala Leu  
 675 680 685  
 Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe Asn  
 690 695 700  
 Phe Arg Ala Pro Pro Asn Ala Leu Pro Glu Asn Leu Leu Arg Lys Gly  
 705 710 715 720  
 Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg Ser  
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 Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu Gln  
 755 760 765  
 Arg His Val Arg Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys His  
 770 775 780  
 Leu Cys Asp Arg Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His Leu  
 785 790 795 800  
 Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser Pro  
 805 810 815  
 His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu Asp  
 820 825 830  
 Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His Gly  
 835 840 845  
 Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met Asn Gly Ser His Phe  
 850 855 860  
 Lys Asp Glu Lys Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu Asp  
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 Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu Asp  
 885 890 895  
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 900 905 910  
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 915 920 925  
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 930 935 940  
 Ser Gly Leu Ser Ala Leu Asp His Ile Arg His Phe Thr Asp Ser Leu  
 945 950 955 960  
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 965 970 975  
 Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu His  
 980 985 990  
 Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser Asp  
 995 1000 1005  
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 His Val

&lt;210&gt; 84

&lt;211&gt; 4039

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 84

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&lt;210&gt; 85

&lt;211&gt; 595

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

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Arg Leu Val Leu Asn Tyr Asp Pro Gly Asp Pro Lys Ala Phe Thr Glu
35      40      45
Ile Asn Arg Leu Leu Pro Tyr Phe Arg Gln Ser Leu Ser Cys Cys Val
50      55      60
Cys Gly His Leu Leu Gln Asp Pro Ile Ala Pro Thr Asn Ser Thr Cys
65      70      75      80
Gln His Tyr Val Cys Lys Thr Cys Lys Gly Lys Lys Met Met Met Lys
85      90      95
Pro Ser Cys Ser Trp Cys Lys Asp Tyr Glu Gln Phe Glu Glu Asn Lys
100     105     110
Gln Leu Ser Ile Leu Val Asn Cys Tyr Lys Lys Leu Cys Glu Tyr Ile
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Thr Gln Thr Thr Leu Ala Arg Asp Ile Ile Glu Ala Val Asp Cys Ser
130     135     140
Ser Asp Ile Leu Ala Leu Leu Asn Asp Gly Ser Leu Phe Cys Glu Glu
145     150     155     160
Thr Glu Lys Pro Ser Asp Ser Ser Phe Thr Leu Cys Leu Thr His Ser
165     170     175
Pro Leu Pro Ser Thr Ser Glu Pro Thr Thr Asp Pro Gln Ala Ser Leu
180     185     190
Ser Pro Met Ser Glu Ser Thr Leu Ser Ile Ala Ile Gly Ser Ser Val
195     200     205
Ile Asn Gly Leu Pro Thr Tyr Asn Gly Leu Ser Ile Asp Arg Phe Gly
210     215     220
Ile Asn Ile Pro Ser Pro Glu His Ser Asn Thr Ile Asp Val Cys Asn
225     230     235     240
Thr Val Asp Ile Lys Thr Glu Asp Leu Ser Asp Ser Leu Pro Pro Val
245     250     255
Cys Asp Thr Val Ala Thr Asp Leu Cys Ser Thr Gly Ile Asp Ile Cys
260     265     270
Ser Phe Ser Glu Asp Ile Lys Pro Gly Asp Ser Leu Leu Leu Ser Val
275     280     285
Glu Glu Val Leu Arg Ser Leu Glu Thr Val Ser Asn Thr Glu Val Cys
290     295     300
Cys Pro Asn Leu Gln Pro Asn Leu Glu Ala Thr Val Ser Asn Gly Pro
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<212> DNA
<213> Homo sapiens
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103

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&lt;210&gt; 87

&lt;211&gt; 252

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 87

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 Lys Ala Ser Asn Val Leu Glu Glu Ile Ala Lys Asp Lys Val Leu Lys  
 35 40 45  
 Asp Phe Tyr Val His Thr Val Met Thr Cys Tyr Phe Ser Leu Phe Gly  
 50 55 60  
 Ile Asp Asn Met Ala Pro Ser Pro Gly His Ile Leu Arg Val Tyr Gly  
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 Gly Val Leu Pro Trp Ser Val Ala Leu Asp Trp Leu Thr Glu Lys Pro  
 85 90 95  
 Glu Leu Phe Gln Leu Ala Leu Lys Ala Phe Arg Tyr Thr Leu Lys Leu  
 100 105 110  
 Met Ile Asp Lys Ala Ser Leu Gly Pro Ile Glu Asp Phe Arg Glu Leu  
 115 120 125  
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 Ser Asp Glu Lys Trp Lys Glu Ala Ile Leu Gln Glu Lys Pro Tyr Leu  
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 Phe Ser Leu Gly Tyr Asp Ser Asn Met Gly Ile Tyr Thr Gly Arg Val  
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&lt;210&gt; 88

&lt;211&gt; 4660

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 88

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&lt;210&gt; 89

&lt;211&gt; 538

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 89

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Ile His Gln Gln Pro Asn Pro Gly Val His Tyr Glu Tyr Val Ile Met
          35          40          45
Gly Thr Asn Ala Ile Ser Pro Gln Val Pro Pro His Arg Arg Pro Gly
          50          55          60
Glu Pro Phe Asn Gly Gln Met Val Thr Glu Gly Arg Ser Gln Glu Glu
          65          70          75          80
Gly Glu Gln Lys Gly Arg Asn Glu Glu Lys Glu Asp Leu Arg Gly Glu
          85          90          95
Ala Pro Glu Met Phe Thr Ser Glu Ser Ala Gln Thr Phe Pro Val Arg
          100          105          110
His Pro Asp Arg Phe Ser Pro His Arg Pro Asp Asn Leu Val Pro Pro
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Ala Pro Gln Pro Pro Arg Arg Ser Arg Asp His Asn Trp Lys Gln Leu
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Gly Thr Thr Glu Cys Ser Thr Thr Cys Gly Lys Gly Ser Gln Tyr Pro
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Tyr Cys Asp Ser Ser Met Lys Pro Thr Pro Glu Glu Glu Pro Cys Asn
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Ile Phe Pro Cys Pro Ala Phe Trp Asp Ile Gly Glu Trp Ser Glu Cys
          195          200          205
Ser Lys Thr Cys Gly Leu Gly Met Gln His Arg Gln Val Leu Cys Arg
          210          215          220
Gln Val Tyr Ala Asn Arg Ser Leu Thr Val Gln Pro Tyr Arg Cys Gln
          225          230          235          240
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          245          250          255
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<211> 4793
<212> DNA
<213> Homo sapiens
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&lt;210&gt; 91

&lt;211&gt; 625

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 91

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Met Ser Gln Glu Ser Asp Asn Asn Lys Arg Leu Val Ala Leu Val Pro
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Met Pro Ser Asp Pro Pro Phe Asn Thr Arg Arg Ala Tyr Thr Ser Glu
          20          25          30
Asp Glu Ala Trp Lys Ser Tyr Leu Glu Asn Pro Leu Thr Ala Ala Thr
          35          40          45
Lys Ala Met Met Ile Ile Asn Gly Asp Glu Asp Ser Ala Ala Ala Leu
          50          55          60
Gly Leu Leu Tyr Asp Tyr Tyr Lys Val Pro Arg Asp Lys Arg Leu Leu
          65          70          75          80
Ser Val Ser Lys Ala Ser Asp Ser Gln Glu Asp Gln Glu Lys Arg Asn
          85          90          95
Cys Leu Gly Thr Ser Glu Ala Gln Ser Asn Leu Ser Gly Gly Glu Asn
          100          105          110
Arg Val Gln Val Leu Lys Thr Val Pro Val Asn Leu Ser Leu Asn Gln
          115          120          125
Asp His Leu Glu Asn Ser Lys Arg Glu Gln Tyr Ser Ile Ser Phe Pro
          130          135          140
Glu Ser Ser Ala Ile Ile Pro Val Ser Gly Ile Thr Val Val Lys Ala
          145          150          155          160
Glu Asp Phe Thr Pro Val Phe Met Ala Pro Pro Val His Tyr Pro Arg
          165          170          175
Gly Asp Gly Glu Gln Arg Val Val Ile Phe Glu Gln Thr Gln Tyr
          180          185          190
Asp Val Pro Ser Leu Ala Thr His Ser Ala Tyr Leu Lys Asp Asp Gln
          195          200          205
Arg Ser Thr Pro Asp Ser Thr Tyr Ser Glu Ser Phe Lys Asp Ala Ala
          210          215          220
Thr Glu Lys Phe Arg Ser Ala Ser Val Gly Ala Glu Glu Tyr Met Tyr
          225          230          235          240
Asp Gln Thr Ser Ser Gly Thr Phe Gln Tyr Thr Leu Glu Ala Thr Lys
          245          250          255
Ser Leu Arg Gln Lys Gln Gly Glu Gly Pro Met Thr Tyr Leu Asn Lys
          260          265          270
Gly Gln Phe Tyr Ala Ile Thr Leu Ser Glu Thr Gly Asp Asn Lys Cys
          275          280          285
Phe Arg His Pro Ile Ser Lys Val Arg Ser Val Val Met Val Val Phe
          290          295          300
Ser Glu Asp Lys Asn Arg Asp Glu Gln Leu Lys Tyr Trp Lys Tyr Trp
          305          310          315          320
His Ser Arg Gln His Thr Ala Lys Gln Arg Val Leu Asp Ile Ala Asp
          325          330          335
Tyr Lys Glu Ser Phe Asn Thr Ile Gly Asn Ile Glu Glu Ile Ala Tyr
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Asn Ala Val Ser Phe Thr Trp Asp Val Asn Glu Glu Ala Lys Ile Phe  
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 Lys Gly Leu Pro Leu Met Ile Gln Ile Asp Thr Tyr Ser Tyr Asn Asn  
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 Arg Ser Asn Lys Pro Ile His Arg Ala Tyr Cys Gln Ile Lys Val Phe  
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 Cys Asp Lys Gly Ala Glu Arg Lys Ile Arg Asp Glu Glu Gln Lys Gln  
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 Asn Arg Lys Asn Gly Lys Gly Gln Ala Ser Gln Thr Gln Cys Asn Ser  
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 Ser Ser Asp Gly Lys Leu Ala Ala Ile Pro Leu Gln Lys Lys Ser Asp  
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 Ile Thr Tyr Phe Lys Thr Met Pro Asp Leu His Ser Gln Pro Val Leu  
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 Phe Ile Pro Asp Val His Phe Ala Asn Leu Gln Arg Thr Gly Gln Val  
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 Tyr Tyr Asn Thr Asp Asp Glu Arg Glu Gly Gly Ser Val Leu Val Lys  
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 Arg Met Phe Arg Pro Met Glu Glu Glu Phe Gly Pro Val Pro Ser Lys  
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 Leu Asn Met Glu Ser Met Val Glu Gly Phe Lys Val Thr Leu Met Glu  
 610 615 620  
 Ile  
 625

&lt;210&gt; 92

&lt;211&gt; 2085

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 92

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&lt;210&gt; 93

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 93

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Arg Ser Leu Cys Glu Ser Glu Glu Gln Arg Leu Leu Glu Gln Val His
          20          25          30
Gly Glu Glu Glu Arg Ala His Gln Ser Ile Leu Thr Gln Arg Val His
          35          40          45
Trp Ala Glu Ala Leu Gln Lys Leu Asp Thr Ile Arg Thr Gly Leu Val
          50          55          60
Gly Met Leu Thr His Leu Asp Asp Leu Gln Leu Ile Gln Lys Glu Gln
          65          70          75          80
Glu Ile Phe Glu Arg Thr Glu Glu Ala Glu Gly Ile Leu Asp Pro Gln
          85          90          95
Glu Ser Glu Met Leu Asn Phe Asn Glu Lys Cys Thr Arg Ser Pro Leu
          100          105          110
Leu Thr Gln Leu Trp Ala Thr Ala Val Leu Gly Ser Leu Ser Gly Thr
          115          120          125
Glu Asp Ile Arg Ile Asp Glu Arg Thr Val Ser Pro Phe Leu Gln Leu
          130          135          140
Ser Asp Asp Arg Lys Thr Leu Thr Phe Ser Thr Lys Lys Ser Lys Ala
          145          150          155          160
Cys Ala Asp Gly Pro Glu Arg Phe Asp His Trp Pro Asn Ala Leu Ala
          165          170          175
Ala Thr Ser Phe Gln Asn Gly Leu His Ala Trp Met Val Asn Val Gln
          180          185          190
Asn Ser Cys Ala Tyr Lys Val Gly Val Ala Ser Gly His Leu Pro Arg
          195          200          205
Lys Gly Ser Gly Ser Asp Cys Arg Leu Gly His Asn Ala Phe Ser Trp
          210          215          220
Val Phe Ser Arg Tyr Asp Gln Glu Phe Arg Phe Ser His Asn Gly Gln
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<210> 95  
<211> 626

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 95

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Pro Trp Pro Gly Leu Pro Leu Pro Ser Leu Val Gly Pro Ala Pro Leu
 20          25          30
Leu Thr Cys Leu Cys Pro Gln Cys Leu Ser Val Glu Asp Ala Leu Gly
 35          40          45
Leu Gly Glu Pro Glu Gly Ser Gly Leu Pro Pro Gly Pro Val Leu Glu
 50          55          60
Ala Arg Tyr Val Ala Arg Leu Ser Ala Ala Ala Val Leu Tyr Leu Ser
 65          70          75          80
Asn Pro Glu Gly Thr Cys Glu Asp Ala Arg Ala Gly Leu Trp Ala Ser
 85          90          95
His Ala Asp His Leu Leu Ala Leu Leu Glu Ser Pro Lys Ala Leu Thr
 100         105         110
Pro Gly Leu Ser Trp Leu Leu Gln Arg Met Gln Ala Arg Ala Ala Gly
 115         120         125
Gln Thr Pro Lys Thr Ala Cys Val Asp Ile Pro Gln Leu Leu Glu Glu
 130         135         140
Ala Val Gly Ala Gly Ala Pro Gly Ser Ala Gly Gly Val Leu Ala Ala
 145         150         155         160
Leu Leu Asp His Val Arg Ser Gly Ser Cys Phe His Ala Leu Pro Ser
 165         170         175
Pro Gln Tyr Phe Val Asp Phe Val Phe Gln Gln His Ser Ser Glu Val
 180         185         190
Pro Met Thr Leu Ala Glu Leu Ser Ala Leu Met Gln Arg Leu Gly Val
 195         200         205
Gly Arg Glu Ala His Ser Asp His Ser His Arg His Arg Gly Ala Ser
 210         215         220
Ser Arg Asp Pro Val Pro Leu Ile Ser Ser Ser Asn Ser Ser Ser Val
 225         230         235         240
Trp Asp Thr Val Cys Leu Ser Ala Arg Asp Val Met Ala Ala Tyr Gly
 245         250         255
Leu Ser Glu Gln Ala Gly Val Thr Pro Glu Ala Trp Ala Gln Leu Ser
 260         265         270
Pro Ala Leu Leu Gln Gln Gln Leu Ser Gly Ala Tyr Thr Ser Gln Ser
 275         280         285
Arg Pro Pro Val Gln Asp Gln Leu Ser Gln Ser Glu Arg Tyr Leu Tyr
 290         295         300
Gly Ser Leu Ala Thr Leu Leu Ile Cys Leu Cys Ala Val Phe Gly Leu
 305         310         315         320
Leu Leu Leu Thr Cys Thr Gly Cys Arg Gly Val Ala His Tyr Ile Leu
 325         330         335
Gln Thr Phe Leu Ser Leu Ala Val Gly Ala Leu Thr Gly Asp Ala Val
 340         345         350
Leu His Leu Thr Pro Lys Val Leu Gly Leu His Thr His Ser Glu Glu
 355         360         365
Gly Leu Ser Pro Gln Pro Thr Trp Arg Leu Leu Ala Met Leu Ala Gly
 370         375         380
Leu Tyr Ala Phe Phe Leu Phe Glu Asn Leu Phe Asn Leu Leu Leu Pro
 385         390         395         400
Arg Asp Pro Glu Asp Leu Glu Asp Gly Pro Cys Gly His Ser Ser His
 405         410         415
Ser His Gly Gly His Ser His Gly Val Ser Leu Gln Leu Ala Pro Ser
 420         425         430

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Glu Leu Arg Gln Pro Lys Pro Pro His Glu Gly Ser Arg Ala Asp Leu  
 435 440 445  
 Val Ala Glu Glu Ser Pro Glu Leu Leu Asn Pro Glu Pro Arg Arg Leu  
 450 455 460  
 Ser Pro Glu Leu Arg Leu Leu Pro Tyr Met Ile Thr Leu Gly Asp Ala  
 465 470 475 480  
 Val His Asn Phe Ala Asp Gly Leu Ala Val Gly Ala Ala Phe Ala Ser  
 485 490 495  
 Ser Trp Lys Thr Gly Leu Ala Thr Ser Leu Ala Val Phe Cys His Glu  
 500 505 510  
 Leu Pro His Glu Leu Gly Asp Phe Ala Ala Leu Leu His Ala Gly Leu  
 515 520 525  
 Ser Val Arg Gln Ala Leu Leu Leu Asn Leu Ala Ser Ala Leu Thr Ala  
 530 535 540  
 Phe Ala Gly Leu Thr Trp His Ser Arg Leu Glu Ser Ala Arg Arg Ala  
 545 550 555 560  
 Arg Pro Gly Ser Trp Gln Trp Pro Pro Ala Cys Ser Leu Arg Ser Thr  
 565 570 575  
 Leu Arg His Ala Pro Gly Asp Val Glu Ser Thr Gly Pro Ala Ala Pro  
 580 585 590  
 Gly Ser Ser Ser Cys Cys Thr Thr Trp Ala Cys Trp Ala Ala Gly Pro  
 595 600 605  
 Ser Cys Cys Cys Cys Pro Cys Thr Arg Met Thr Ser Pro Ser Asp Thr  
 610 615 620  
 Leu Pro  
 625

&lt;210&gt; 96

&lt;211&gt; 2761

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 96

agcgggctct gcagagaaat caaagatggc ggttgatatct gctgttcgct ggctgggcct 60  
 ccgcagcagg cttggccagc cgctgacggg tcggcgggcg ggtttgtgtg aacaggcacg 120  
 cagctgcaga ttttattctg gtatgtcaac cctctcaaag gttgaaggaa ctgatgtaac 180  
 agggattgaa gaagtagtaa ttccaaaaaa gaaaacttgg gataaagtag ccgttcttca 240  
 ggcacttgca tccacagtaa acagggatac cacagctgtg ccttatgtgt ttcaagatga 300  
 tccttacctt atgccagcat catcttttga atctcgttca tttttactgg caaagaaatc 360  
 cggggagaat gtggccaagt ttattattaa ttcatacccc aaatatattc agaaggacat 420  
 agctgaacct catataccgt gtttaatgcc tgagtacttt gaacctcaga tcaaagacat 480  
 aagtgaagcc gccctgaagg aacgaattga gtcagaaaa gtcaaagcct ctgtggacat 540  
 gtttgatcag cttttgcaag caggaaccac tgtgtctctt gaaacaacaa atagtctctt 600  
 ggatttattg tgttactatg gtgaccagga gccctcaact gattaccatt ttcaacaac 660  
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 tcagtttgga gttacatggc gagcaaaaaa caacgctgag agaattcttt ctctaattgc 780  
 agagaaaaat gaacattcct attgcacaat gatccgagga atggtgaagc accgagctta 840  
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gccgctgcc tagttttcta acttgaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2760
a                                                                 2761

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&lt;210&gt; 97

&lt;211&gt; 422

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 97

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Ala Gly Ser Ala Glu Lys Ser Lys Met Ala Val Val Ser Ala Val Arg
 1              5              10              15
Trp Leu Gly Leu Arg Ser Arg Leu Gly Gln Pro Leu Thr Gly Arg Arg
 20              25              30
Ala Gly Leu Cys Glu Gln Ala Arg Ser Cys Arg Phe Tyr Ser Gly Ser
 35              40              45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
 50              55              60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
 65              70              75              80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
 85              90              95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
100              105              110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
115              120              125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
130              135              140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
145              150              155              160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
165              170              175
Ser Val Asp Met Phe Asp Gln Leu Leu Glu Ala Gly Thr Thr Val Ser
180              185              190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
195              200              205
Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
210              215              220

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115

Ala Leu Glu Glu Glu Asn Asp Glu Thr Ser Arg Arg Lys Ala Gly His  
 225 230 235 240  
 Gln Phe Gly Val Thr Trp Arg Ala Lys Asn Asn Ala Glu Arg Ile Phe  
 245 250 255  
 Ser Leu Met Pro Glu Lys Asn Glu His Ser Tyr Cys Thr Met Ile Arg  
 260 265 270  
 Gly Met Val Lys His Arg Ala Tyr Glu Gln Ala Leu Asn Leu Tyr Thr  
 275 280 285  
 Glu Leu Leu Asn Asn Arg Leu His Ala Asp Val Tyr Thr Phe Asn Ala  
 290 295 300  
 Leu Ile Glu Ala Thr Val Cys Ala Ile Asn Glu Lys Phe Glu Glu Lys  
 305 310 315 320  
 Trp Ser Lys Ile Leu Glu Leu Leu Arg His Met Val Ala Gln Lys Val  
 325 330 335  
 Lys Pro Asn Leu Gln Thr Phe Asn Thr Ile Leu Lys Cys Leu Arg Arg  
 340 345 350  
 Phe His Val Phe Ala Arg Ser Pro Ala Leu Gln Val Leu Arg Glu Met  
 355 360 365  
 Lys Ala Ile Gly Ile Glu Pro Ser Leu Ala Thr Tyr His His Ile Ile  
 370 375 380  
 Arg Leu Phe Asp Gln Pro Gly Asp Pro Leu Lys Arg Ser Ser Phe Ile  
 385 390 395 400  
 Ile Tyr Asp Ile Met Asn Glu Leu Met Gly Lys Arg Phe Ser Pro Lys  
 405 410 415  
 Asp Pro Asp Asp Gly Ile  
 420

&lt;210&gt; 98

&lt;211&gt; 2757

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 98

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 cagctgcaga ttttattctg gtatgcaac cctctcaaag gttgaaggaa ctgatgtaac 180  
 agggattgaa gaagtagtaa ttccaaaaaa gaaaacttgg gataaagtag ccgttcttca 240  
 ggcacttgca tccacagtaa acagggatac cacagctgtg ccttatgtgt ttcaagatga 300  
 tccttacctt atgccagcat catctttgga atctcgttca tttttactgg caaagaaatc 360  
 cggggagaat gtggccaagt ttattattaa ttcatacccc aaatattttc agaaggacat 420  
 agctgaacct catataccgt gtttaatgcc tgagtacttt gaacctcaga tcaaagacat 480  
 aagtgaagcc gccctgaagg aacgaattga gctcagaaaa gtcaaagcct ctgtggacat 540  
 gtttgatcag cttttgcaag caggaaccac tgtgtctctt gaaacaacaa atagtctctt 600  
 ggatttattg tgttactatg gtgaccagga gccctcaact gattaccatt ttcaacaaac 660  
 tggacagtca gaagcattgg aagaggaaaa tgatgagaca tctaggagga aagctggtca 720  
 tcagtttgga gttacatggc gagcaaaaaa caacgctgag agaactcttt ctctaattgcc 780  
 agagaaaaat gaacattcct attgcacaat gatccgagga atggtgaagc accgagctta 840  
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 cacatttaat gcattgattg aagcaacagt atgtgcgata aatgagaaat ttgaggaaaa 960  
 atggagtaaa atactggagc tgctaagaca catggttgca cagaaggtga aaccaaatct 1020  
 tcagactttt aataccattc tgaaatgtct ccgaagattt catgtgtttg caagatcgcc 1080  
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 ctaccaagta catggccttt taaaaaccgg agacaactgg aaattcattg gacctgatca 1380  
 acatcgtaat ttctattatt ccaagttctt cgatttgatt tgtctaattg aacaaattga 1440

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cagtatact gacagcagca gtgacagcga cagtgcaccc agtgaaggca aatgaaagtg 2100
gagattcagg agcagcaatg gtctcaccat agctgctgga atcacacctg agaactgaga 2160
tataccaata tttaacattg ttacaaagaa gaaaagatac agatttggtg aatttggtac 2220
tgtgaggtac agtcagtaca cagctgactt atgtagattt aagctgctaa tatgctactt 2280
aaccatctat taatgcacca ttaaaggctt agcatttaag tagcaacatt gcggttttca 2340
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cctttgttgg cctgatgtgc tgctgtgatg ctggctcttc atcttaggtg ttcatgcagt 2520
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ataacgcatac ttaggaatga ctaaacaaga taatggcagt ttaggctgca caactggtaa 2640
aatgactgta gataaatgtt gtaattagtg tacacgtttg tatttttgtt aatatagccg 2700
ctgccatagt tttctaactt gaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaa 2757

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&lt;210&gt; 99

&lt;211&gt; 697

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 99

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Ala Gly Ser Ala Glu Lys Ser Lys Met Ala Val Val Ser Ala Val Arg
 1          5          10          15
Trp Leu Gly Leu Arg Ser Arg Leu Gly Gln Pro Leu Thr Gly Arg Arg
 20          25          30
Ala Gly Leu Cys Glu Gln Ala Arg Ser Cys Arg Phe Tyr Ser Gly Ser
 35          40          45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
 50          55          60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
 65          70          75          80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
 85          90          95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
100          105          110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
115          120          125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
130          135          140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
145          150          155          160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
165          170          175
Ser Val Asp Met Phe Asp Gln Leu Leu Gln Ala Gly Thr Thr Val Ser
180          185          190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
195          200          205
Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
210          215          220
Ala Leu Glu Glu Glu Asn Asp Glu Thr Ser Arg Arg Lys Ala Gly His

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225 230 235 240  
 Gln Phe Gly Val Thr Trp Arg Ala Lys Asn Asn Ala Glu Arg Ile Phe  
 245 250 255  
 Ser Leu Met Pro Glu Lys Asn Glu His Ser Tyr Cys Thr Met Ile Arg  
 260 265 270  
 Gly Met Val Lys His Arg Ala Tyr Glu Gln Ala Leu Asn Leu Tyr Thr  
 275 280 285  
 Glu Leu Leu Asn Asn Arg Leu His Ala Asp Val Tyr Thr Phe Asn Ala  
 290 295 300  
 Leu Ile Glu Ala Thr Val Cys Ala Ile Asn Glu Lys Phe Glu Glu Lys  
 305 310 315 320  
 Trp Ser Lys Ile Leu Glu Leu Leu Arg His Met Val Ala Gln Lys Val  
 325 330 335  
 Lys Pro Asn Leu Gln Thr Phe Asn Thr Ile Leu Lys Cys Leu Arg Arg  
 340 345 350  
 Phe His Val Phe Ala Arg Ser Pro Ala Leu Gln Val Leu Arg Glu Met  
 355 360 365  
 Lys Ala Ile Gly Ile Glu Pro Ser Leu Ala Thr Tyr His His Ile Ile  
 370 375 380  
 Arg Leu Phe Asp Gln Pro Gly Asp Pro Leu Lys Arg Ser Ser Phe Ile  
 385 390 395 400  
 Ile Tyr Asp Ile Met Asn Glu Leu Met Gly Lys Arg Phe Ser Pro Lys  
 405 410 415  
 Asp Pro Asp Asp Asp Lys Phe Phe Gln Ser Ala Met Ser Ile Cys Ser  
 420 425 430  
 Ser Leu Arg Asp Leu Glu Leu Ala Tyr Gln Val His Gly Leu Leu Lys  
 435 440 445  
 Thr Gly Asp Asn Trp Lys Phe Ile Gly Pro Asp Gln His Arg Asn Phe  
 450 455 460  
 Tyr Tyr Ser Lys Phe Phe Asp Leu Ile Cys Leu Met Glu Gln Ile Asp  
 465 470 475 480  
 Val Thr Leu Lys Trp Tyr Glu Asp Leu Ile Pro Ser Ala Tyr Phe Pro  
 485 490 495  
 His Ser Gln Thr Met Ile His Leu Leu Gln Ala Leu Asp Val Ala Asn  
 500 505 510  
 Arg Leu Glu Val Ile Pro Lys Ile Trp Lys Asp Ser Lys Glu Tyr Gly  
 515 520 525  
 His Thr Phe Arg Ser Asp Leu Arg Glu Glu Ile Leu Met Leu Met Ala  
 530 535 540  
 Arg Asp Lys His Pro Pro Glu Leu Gln Val Ala Phe Ala Asp Cys Ala  
 545 550 555 560  
 Ala Asp Ile Lys Ser Ala Tyr Glu Ser Gln Pro Ile Arg Gln Thr Ala  
 565 570 575  
 Gln Asp Trp Pro Ala Thr Ser Leu Asn Cys Ile Ala Ile Leu Phe Leu  
 580 585 590  
 Arg Ala Gly Arg Thr Gln Glu Ala Trp Lys Met Leu Gly Leu Phe Arg  
 595 600 605  
 Lys His Asn Lys Ile Pro Arg Ser Glu Leu Leu Asn Glu Leu Met Asp  
 610 615 620  
 Ser Ala Lys Val Ser Asn Ser Pro Ser Gln Ala Ile Glu Val Val Glu  
 625 630 635 640  
 Leu Ala Ser Ala Phe Ser Leu Pro Ile Cys Glu Gly Leu Thr Gln Arg  
 645 650 655  
 Val Met Ser Asp Phe Ala Ile Asn Gln Glu Gln Lys Glu Ala Leu Ser  
 660 665 670  
 Asn Leu Thr Ala Leu Thr Ser Asp Ser Asp Thr Asp Ser Ser Ser Asp  
 675 680 685  
 Ser Asp Ser Asp Thr Ser Glu Gly Lys

690

695

&lt;210&gt; 100

&lt;211&gt; 1940

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 100

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tacatggcga gcaaaaaaac aacgctgaga gaatcttttc tctaatagcc gagaaaaatg 60
aacattccta ttgcacaatg atccgaggaa tggatgaagct gatgtatata catttaatgc 120
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&lt;210&gt; 101

&lt;211&gt; 280

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 101

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Met Met Ala Tyr Lys Phe Phe Gln Ser Ala Met Ser Ile Cys Ser Ser
1           5           10          15
Leu Arg Asp Leu Glu Leu Ala Tyr Gln Val His Gly Leu Leu Lys Thr
20          25          30
Gly Asp Asn Trp Lys Phe Ile Gly Pro Asp Gln His Arg Asn Phe Tyr
35          40          45
Tyr Ser Lys Phe Phe Asp Leu Ile Cys Leu Met Glu Gln Ile Asp Val
50          55          60
Thr Leu Lys Trp Tyr Glu Asp Leu Ile Pro Ser Ala Tyr Phe Pro His

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65		70		75		80
Ser Gln Thr Met	Ile His Leu Leu Gln	Ala Leu Asp Val	Ala Asn Arg			
	85	90	95			
Leu Glu Val Ile	Pro Lys Ile Trp	Lys Asp Ser Lys	Glu Tyr Gly His			
	100	105	110			
Thr Phe Arg Ser	Asp Leu Arg Glu	Glu Ile Leu Met	Leu Met Ala Arg			
	115	120	125			
Asp Lys His Pro	Pro Glu Leu Gln	Val Ala Phe Ala	Asp Cys Ala Ala			
	130	135	140			
Asp Ile Lys Ser	Ala Tyr Glu Ser	Gln Pro Ile Arg	Gln Thr Ala Gln			
	145	150	155			160
Asp Trp Pro Ala	Thr Ser Leu Asn	Cys Ile Ala Ile	Leu Phe Leu Arg			
	165	170	175			
Ala Gly Arg Thr	Gln Glu Ala Trp	Lys Met Leu Gly	Leu Phe Arg Lys			
	180	185	190			
His Asn Lys Ile	Pro Arg Ser Glu	Leu Leu Asn Glu	Leu Met Asp Ser			
	195	200	205			
Ala Lys Val Ser	Asn Ser Pro Ser	Gln Ala Ile Glu	Val Val Glu Leu			
	210	215	220			
Ala Ser Ala Phe	Ser Leu Pro Ile	Cys Glu Gly Leu	Thr Gln Arg Val			
	225	230	235			240
Met Ser Asp Phe	Ala Ile Asn Gln	Glu Gln Lys Glu	Ala Leu Ser Asn			
	245	250	255			
Leu Thr Ala Leu	Thr Ser Asp Ser	Asp Thr Asp Ser	Ser Ser Ser Asp			
	260	265	270			
Asp Ser Asp Thr	Ser Glu Gly Lys					
	275	280				

&lt;210&gt; 102

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

```

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120

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```

&lt;210&gt; 103

&lt;211&gt; 414

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

```

Met Ser Ser Pro Asp Ala Gly Tyr Ala Ser Asp Asp Gln Ser Gln Thr
1      5      10      15
Gln Ser Ala Leu Pro Ala Val Met Ala Gly Leu Gly Pro Cys Pro Trp
20     25     30
Ala Glu Ser Leu Ser Pro Ile Gly Asp Met Lys Val Lys Gly Glu Ala
35     40     45
Pro Ala Asn Ser Gly Ala Pro Ala Gly Ala Ala Gly Arg Ala Lys Gly
50     55     60
Glu Ser Arg Ile Arg Arg Pro Met Asn Ala Phe Met Val Trp Ala Lys
65     70     75     80
Asp Glu Arg Lys Arg Leu Ala Gln Gln Asn Pro Asp Leu His Asn Ala
85     90     95
Glu Leu Ser Lys Met Leu Gly Lys Ser Trp Lys Ala Leu Thr Leu Ala
100    105    110
Glu Lys Arg Pro Phe Val Glu Glu Ala Glu Arg Leu Arg Val Gln His
115    120    125
Met Gln Asp His Pro Asn Tyr Lys Tyr Arg Pro Arg Arg Arg Lys Gln
130    135    140
Val Lys Arg Leu Lys Arg Val Glu Gly Gly Phe Leu His Gly Leu Ala
145    150    155    160
Glu Pro Gln Ala Ala Ala Leu Gly Pro Glu Gly Gly Arg Val Ala Met
165    170    175
Asp Gly Leu Gly Leu Gln Phe Pro Glu Gln Gly Phe Pro Ala Gly Pro
180    185    190
Pro Leu Leu Pro Pro His Met Gly Gly His Tyr Arg Asp Cys Gln Ser
195    200    205
Leu Gly Ala Pro Pro Leu Asp Gly Tyr Pro Leu Pro Thr Pro Asp Thr
210    215    220
Ser Pro Leu Asp Gly Val Asp Pro Asp Pro Ala Phe Phe Ala Ala Pro
225    230    235    240
Met Pro Gly Asp Cys Pro Ala Ala Gly Thr Tyr Ser Tyr Ala Gln Val
245    250    255
Ser Asp Tyr Ala Gly Pro Pro Glu Pro Pro Ala Gly Pro Met His Pro
260    265    270
Arg Leu Gly Pro Glu Pro Ala Gly Pro Ser Ile Pro Gly Leu Leu Ala
275    280    285
Pro Pro Ser Ala Leu His Val Tyr Tyr Gly Ala Met Gly Ser Pro Gly
290    295    300
Ala Gly Gly Gly Arg Gly Phe Gln Met Gln Pro Gln His Gln His Gln
305    310    315    320
His Gln His Gln His His Pro Pro Gly Pro Gly Gln Pro Ser Pro Pro
325    330    335
Pro Glu Ala Leu Pro Cys Arg Asp Gly Thr Asp Pro Ser Gln Pro Ala

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	340		345		350										
Glu	Leu	Leu	Gly	Glu	Val	Asp	Arg	Thr	Glu	Phe	Glu	Gln	Tyr	Leu	His
	355						360					365			
Phe	Val	Cys	Lys	Pro	Glu	Met	Gly	Leu	Pro	Tyr	Gln	Gly	His	Asp	Ser
	370						375					380			
Gly	Val	Asn	Leu	Pro	Asp	Ser	His	Gly	Ala	Ile	Ser	Ser	Val	Val	Ser
	385						390					395			400
Asp	Ala	Ser	Ser	Ala	Val	Tyr	Tyr	Cys	Asn	Tyr	Pro	Asp	Val		
			405						410						

&lt;210&gt; 104

&lt;211&gt; 2398

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

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```

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 <211> 232  
 <212> PRT  
 <213> Homo sapiens

<400> 105  
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 Met Glu Lys Thr Pro His Cys Phe Leu Thr Asp Gln Gly Ala Ala Gln  
 35 40 45  
 Phe Ala Ala Ala Met Gly Val Pro Glu Ile Pro Gly Glu Lys Leu Val  
 50 55 60  
 Thr Glu Arg Asn Lys Lys Arg Leu Glu Lys Glu Lys His Glu Lys Gly  
 65 70 75 80  
 Ala Gln Lys Thr Asp Cys Gln Lys Asn Leu Gly Thr Val Gly Ala Val  
 85 90 95  
 Ala Leu Asp Cys Lys Gly Asn Val Ala Tyr Ala Thr Ser Thr Gly Gly  
 100 105 110  
 Ile Val Asn Lys Met Val Gly Arg Val Gly Asp Ser Pro Cys Leu Gly  
 115 120 125  
 Ala Gly Gly Tyr Ala Asp Asn Asp Ile Gly Ala Val Ser Thr Thr Gly  
 130 135 140  
 His Gly Glu Ser Ile Leu Lys Val Asn Leu Ala Arg Leu Thr Leu Phe  
 145 150 155 160  
 His Ile Glu Gln Gly Lys Thr Val Glu Glu Ala Ala Asp Leu Ser Leu  
 165 170 175  
 Gly Tyr Met Lys Ser Arg Val Lys Gly Leu Gly Gly Leu Ile Val Val  
 180 185 190  
 Ser Lys Thr Gly Asp Trp Val Ala Lys Trp Thr Ser Thr Ser Met Pro  
 195 200 205  
 Trp Ala Ala Ala Lys Asp Gly Lys Leu His Phe Gly Ile Asp Pro Asp  
 210 215 220  
 Asp Thr Thr Ile Thr Asp Leu Pro  
 225 230

<210> 106  
 <211> 1811  
 <212> DNA  
 <213> Homo sapiens

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 cacagtcact actgtgcct cagctgggaa cattggggag gatggaatcc agagctgcac 240  
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aaactgattt tagagttctg atcgttcaag agaatgatta aatatacatt tcctaaaaaa 1800
aaaaaaaaa a 1811

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&lt;210&gt; 107

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

```

Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1      5      10      15
Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20     25     30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35     40     45
Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50     55     60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65     70     75     80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85     90     95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100    105    110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115    120    125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130    135    140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145    150    155    160
Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
165    170    175
Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180    185    190
Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195    200    205
Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210    215    220
Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225    230    235    240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
245    250    255
Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
260    265    270

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Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys  
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<210> 108  
<211> 2611  
<212> DNA  
<213> Homo sapiens

<400> 108  
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aaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 2611

<210> 109  
<211> 150  
<212> PRT



125

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

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Gln Asn Leu Ala Cys Phe Leu Thr Asn Pro His Cys Gly Ser Leu Val
      20           25           30
Asn Ala Asp Gly His Gly Glu Val Trp Thr Asp Trp Asn Asn Met Ser
 35           40           45
Lys Phe Phe Gln Tyr Gly Trp Arg Cys Thr Thr Asn Glu Asn Thr Tyr
 50           55           60
Ser Asn Arg Thr Leu Met Gly Asn Trp Asn Gln Glu Arg Tyr Asp Leu
 65           70           75           80
Arg Asn Ile Val Gln Pro Lys Pro Leu Pro Ser Gln Phe Gly His Tyr
      85           90           95
Phe Glu Thr Thr Tyr Asp Thr Ser Tyr Asn Asn Lys Met Pro Leu Ser
      100           105           110
Thr His Arg Phe Lys Arg Glu Pro His Trp Phe Pro Gly His Gln Pro
      115           120           125
Glu Leu Asp Pro Pro Arg Tyr Lys Cys Thr Glu Lys Ser Thr Tyr Met
      130           135           140
Asn Ser Tyr Ser Lys Pro
145           150

```

&lt;210&gt; 110

&lt;211&gt; 1032

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

```

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aaccagacac cg                                     1032

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&lt;210&gt; 111

&lt;211&gt; 257

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

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Met Ala Gln Arg Met Thr Thr Gln Leu Leu Leu Leu Val Trp Val
 1           5           10           15

```

126.

Ala Val Val Gly Glu Ala Gln Thr Arg Ile Ala Trp Ala Arg Thr Glu  
 20 25 30  
 Leu Leu Asn Val Cys Met Asn Ala Lys His His Lys Glu Lys Pro Gly  
 35 40 45  
 Pro Glu Asp Lys Leu His Glu Gln Cys Arg Pro Trp Arg Lys Asn Ala  
 50 55 60  
 Cys Cys Ser Thr Asn Thr Ser Gln Glu Ala His Lys Asp Val Ser Tyr  
 65 70 75 80  
 Leu Tyr Arg Phe Asn Trp Asn His Cys Gly Glu Met Ala Pro Ala Cys  
 85 90 95  
 Lys Arg His Phe Ile Gln Asp Thr Cys Leu Tyr Glu Cys Ser Pro Asn  
 100 105 110  
 Leu Gly Pro Trp Ile Gln Gln Val Asp Gln Ser Trp Arg Lys Glu Arg  
 115 120 125  
 Val Leu Asn Val Pro Leu Cys Lys Glu Asp Cys Glu Gln Trp Trp Glu  
 130 135 140  
 Asp Cys Arg Thr Ser Tyr Thr Cys Lys Ser Asn Trp His Lys Gly Trp  
 145 150 155 160  
 Asn Trp Thr Ser Gly Phe Asn Lys Cys Ala Val Gly Ala Ala Cys Gln  
 165 170 175  
 Pro Phe His Phe Tyr Phe Pro Thr Pro Thr Val Leu Cys Asn Glu Ile  
 180 185 190  
 Trp Thr His Ser Tyr Lys Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg  
 195 200 205  
 Cys Ile Gln Met Trp Phe Asp Pro Ala Gln Gly Asn Pro Asn Glu Glu  
 210 215 220  
 Val Ala Arg Phe Tyr Ala Ala Ala Met Ser Gly Ala Gly Pro Trp Ala  
 225 230 235 240  
 Ala Trp Pro Phe Leu Leu Ser Leu Ala Leu Met Leu Leu Trp Leu Leu  
 245 250 255  
 Ser

&lt;210&gt; 112

&lt;211&gt; 1104

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 112

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ccactttgaa taaaccagac accg

1104

&lt;210&gt; 113

&lt;211&gt; 939

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

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tggaaccact	gtggagagat	ggcacctgcc	tgcaaacggc	atttcatcca	ggacacctgc	360
ctctacagat	gtccccccaa	cttggggccc	tggatccagc	aggtggatca	gagctggcgc	420
aaagagcggg	tactgaacgt	gcccctgtgc	aaagaggact	gtgagcaatg	gtgggaagat	480
tgctgcacct	cctacacctg	caagagcaac	tggcacaagg	gctggaactg	gacttcaggg	540
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actgttctgt	gcaatgaaat	ctggactcac	tcctacaagg	tcagcaacta	cagccgaggg	660
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&lt;210&gt; 114

&lt;211&gt; 1331

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 114

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tccctactgt	gtgacttggg	gcatggccct	catctgtgct	gaaatgattc	cacaaagatt	180
aaactggcta	tcatttgttg	atttccccct	tcttacattt	aatccttgca	ggagaaagct	240
aagcctcaag	atagtttgct	tctctttccc	ccaaggccaa	ggagaagggt	gagtgagggc	300
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&lt;210&gt; 115

&lt;211&gt; 929

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 115

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tcgaccctgg aggaagaatg cctgctgttc taccaacacc agccaggaag cccataagga 240
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accgcacatg tgtcttgaga attatttgg 929

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&lt;210&gt; 116

&lt;211&gt; 858

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 116

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ccacatgaaa aaaaaaaaa 858

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&lt;210&gt; 117

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 117

```

Met Ala Trp Gln Met Met Gln Leu Leu Leu Leu Ala Leu Val Thr Ala
1           5           10          15
Ala Gly Ser Ala Gln Pro Arg Ser Ala Arg Ala Arg Thr Asp Leu Leu
20          25          30
Asn Val Cys Met Asn Ala Lys His His Lys Thr Gln Pro Ser Pro Glu
35          40          45
Asp Glu Leu Tyr Gly Gln Cys Ser Pro Trp Lys Lys Asn Ala Cys Cys
50          55          60
Thr Ala Ser Thr Ser Gln Glu Leu His Lys Asp Thr Ser Arg Leu Tyr
65          70          75          80

```

129

Asn Phe Asn Trp Asp His Cys Gly Lys Met Glu Pro Thr Cys Lys Arg  
                   85                                  90                                  95  
 His Phe Ile Gln Asp Ser Cys Leu Tyr Glu Cys Ser Pro Asn Leu Gly  
                   100                                  105                                  110  
 Pro Trp Ile Arg Gln Val Asn Gln Ser Trp Arg Lys Glu Arg Ile Leu  
                   115                                  120                                  125  
 Asn Val Pro Leu Cys Lys Glu Asp Cys Glu Arg Trp Trp Glu Asp Cys  
                   130                                  135                                  140  
 Arg Thr Ser Tyr Thr Cys Lys Ser Asn Trp His Lys Gly Trp Asn Trp  
                   145                                  150                                  155                                  160  
 Thr Ser Gly Ile Asn Glu Cys Pro Ala Gly Ala Leu Cys Ser Thr Phe  
                   165                                  170                                  175  
 Glu Ser Tyr Phe Pro Thr Pro Ala Ala Leu Cys Glu Gly Leu Trp Ser  
                   180                                  185                                  190  
 His Ser Phe Lys Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg Cys Ile  
                   195                                  200                                  205  
 Gln Met Trp Phe Asp Ser Ala Gln Gly Asn Pro Asn Glu Glu Val Ala  
                   210                                  215                                  220  
 Lys Phe Tyr Ala Ala Ala Met Asn Ala Gly Ala Pro Ser Arg Gly Ile  
                   225                                  230                                  235                                  240  
 Ile Asp Ser

&lt;210&gt; 118

&lt;211&gt; 1362

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 118

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&lt;210&gt; 119

&lt;211&gt; 453

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 119

Met Ala Ser Pro Ser Leu Pro Gly Ser Asp Cys Ser Gln Ile Ile Asp  
 1 5 10 15  
 His Ser His Val Pro Glu Phe Glu Val Ala Thr Trp Ile Lys Ile Thr  
 20 25 30  
 Leu Ile Leu Val Tyr Leu Ile Ile Phe Val Met Gly Leu Leu Gly Asn  
 35 40 45  
 Ser Ala Thr Ile Arg Val Thr Gln Val Leu Gln Lys Lys Gly Tyr Leu  
 50 55 60  
 Gln Lys Glu Val Thr Asp His Met Val Ser Leu Ala Cys Ser Asp Ile  
 65 70 75 80  
 Leu Val Phe Leu Ile Gly Met Pro Met Glu Phe Tyr Ser Ile Ile Trp  
 85 90 95  
 Asn Pro Leu Thr Thr Ser Ser Tyr Thr Leu Ser Cys Lys Leu His Thr  
 100 105 110  
 Phe Leu Phe Glu Ala Cys Ser Tyr Ala Thr Leu Leu His Val Leu Thr  
 115 120 125  
 Leu Ser Phe Glu Arg Tyr Ile Ala Ile Cys His Pro Phe Arg Tyr Lys  
 130 135 140  
 Ala Val Ser Gly Pro Cys Gln Val Lys Leu Leu Ile Gly Phe Val Trp  
 145 150 155 160  
 Val Thr Ser Ala Leu Val Ala Leu Pro Leu Leu Phe Ala Met Gly Thr  
 165 170 175  
 Glu Tyr Pro Leu Val Asn Val Pro Ser His Arg Gly Leu Thr Cys Asn  
 180 185 190  
 Arg Ser Ser Thr Arg His His Glu Gln Pro Glu Thr Ser Asn Met Ser  
 195 200 205  
 Ile Cys Thr Asn Leu Ser Ser Arg Trp Thr Val Phe Gln Ser Ser Ile  
 210 215 220  
 Phe Gly Ala Phe Val Val Tyr Leu Val Val Leu Leu Ser Val Ala Phe  
 225 230 235 240  
 Met Cys Trp Asn Met Met Gln Val Leu Met Lys Ser Gln Lys Gly Ser  
 245 250 255  
 Leu Ala Gly Gly Thr Arg Pro Pro Gln Leu Arg Lys Ser Glu Ser Glu  
 260 265 270  
 Glu Ser Arg Thr Ala Arg Arg Gln Thr Ile Ile Phe Leu Arg Leu Ile  
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 Val Val Thr Leu Ala Val Cys Trp Met Pro Asn Gln Ile Arg Arg Ile  
 290 295 300  
 Met Ala Ala Ala Lys Pro Lys His Asp Trp Thr Arg Ser Tyr Phe Arg  
 305 310 315 320  
 Ala Tyr Met Ile Leu Leu Pro Phe Ser Glu Thr Phe Phe Tyr Leu Ser  
 325 330 335  
 Ser Val Ile Asn Pro Leu Leu Tyr Thr Val Ser Ser Gln Gln Phe Arg  
 340 345 350  
 Arg Val Phe Val Gln Val Leu Cys Cys Arg Leu Ser Leu Gln His Ala  
 355 360 365  
 Asn His Glu Lys Arg Leu Arg Val His Ala His Ser Thr Thr Asp Ser  
 370 375 380  
 Ala Arg Phe Val Gln Arg Pro Leu Leu Phe Ala Ser Arg Arg Gln Ser  
 385 390 395 400  
 Ser Ala Arg Arg Thr Glu Lys Ile Phe Leu Ser Thr Phe Gln Ser Glu  
 405 410 415  
 Ala Glu Pro Gln Ser Lys Ser Gln Ser Leu Ser Leu Glu Ser Leu Glu  
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 Pro Asn Ser Gly Ala Lys Pro Ala Asn Ser Ala Ala Glu Asn Gly Phe  
 435 440 445

Gln Glu His Glu Val  
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<210> 120  
<211> 2870  
<212> DNA  
<213> Homo sapiens

<400> 120

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tcagagagaa agatgagagc tcaccagggt ctcaccttcc tcctgctctt cgtgatcacc 180
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tagcagggtc tcagggttcc ccactaggat gcagagatga cctctcgctg cctcacaagc 2340
agtgcacct cgggtccttt ccgttgctat ggtgaaaatt cctggatgga atggatcaca 2400
tgagggtttc ttgttgcttt tggagggtgt gggggatatt ttgttttgg ttttctgcag 2460
gttccatgaa aacagccctt ttccaagccc attgtttctg tcatggtttc catctgtcct 2520
gagcaagtca ttcttttgtt atttagcatt tcgaacatct cggccattca aagcccccat 2580
gttctctgca ctgtttggcc agcataacct ctgcatcgaa ttcaaagcag agttttaacc 2640
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tgctttttct ataaaactac ccataagcct ttaaccttta aagaaaaatg aaaaaggtta 2760
gtgtttgggg gccgggggag gactgaccgc ttcataagcc agtacgtctg agctgagtat 2820
gtttcaataa accttttgat atttctcaaa aaaaaaaaaa aaaaaaaaaa 2870
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<210> 121
<211> 403
<212> PRT
<213> Homo sapiens
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<400> 121

Met	Phe	Val	Ala	Ser	Glu	Arg	Lys	Met	Arg	Ala	His	Gln	Val	Leu	Thr
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Phe	Leu	Leu	Leu	Phe	Val	Ile	Thr	Ser	Val	Ala	Ser	Glu	Asn	Ala	Ser
			20					25					30		
Thr	Ser	Arg	Gly	Cys	Gly	Leu	Asp	Leu	Leu	Pro	Gln	Tyr	Val	Ser	Leu
		35					40					45			
Cys	Asp	Leu	Asp	Ala	Ile	Trp	Gly	Ile	Val	Val	Glu	Ala	Val	Ala	Gly
	50					55					60				
Ala	Gly	Ala	Leu	Ile	Thr	Leu	Leu	Leu	Met	Leu	Ile	Leu	Leu	Val	Arg
65					70					75					80
Leu	Pro	Phe	Ile	Lys	Glu	Lys	Glu	Lys	Lys	Ser	Pro	Val	Gly	Leu	His
				85					90					95	
Phe	Leu	Phe	Leu	Leu	Gly	Thr	Leu	Gly	Leu	Phe	Gly	Leu	Thr	Phe	Ala
			100					105					110		
Phe	Ile	Ile	Gln	Glu	Asp	Glu	Thr	Ile	Cys	Ser	Val	Arg	Arg	Phe	Leu
		115					120					125			
Trp	Gly	Val	Leu	Phe	Ala	Leu	Cys	Phe	Ser	Cys	Leu	Leu	Ser	Gln	Ala
	130				135						140				
Trp	Arg	Val	Arg	Arg	Leu	Val	Arg	His	Gly	Thr	Gly	Pro	Ala	Gly	Trp
145					150					155					160
Gln	Leu	Val	Gly	Leu	Ala	Leu	Cys	Leu	Met	Leu	Val	Gln	Val	Ile	Ile
				165					170					175	
Ala	Val	Glu	Trp	Leu	Val	Leu	Thr	Val	Leu	Arg	Asp	Thr	Arg	Pro	Ala
			180					185					190		
Cys	Ala	Tyr	Glu	Pro	Met	Asp	Phe	Val	Met	Ala	Leu	Ile	Tyr	Asp	Met
		195					200					205			
Val	Leu	Leu	Val	Val	Thr	Leu	Gly	Leu	Ala	Leu	Phe	Thr	Leu	Cys	Gly
		210				215					220				
Lys	Phe	Lys	Arg	Trp	Lys	Leu	Asn	Gly	Ala	Phe	Leu	Leu	Ile	Thr	Ala
225					230					235					240
Phe	Leu	Ser	Val	Leu	Ile	Trp	Val	Ala	Trp	Met	Thr	Met	Tyr	Leu	Phe
				245					250					255	
Gly	Asn	Val	Lys	Leu	Gln	Gln	Gly	Asp	Ala	Trp	Asn	Asp	Pro	Thr	Leu
			260					265					270		
Ala	Ile	Thr	Leu	Ala	Ala	Ser	Gly	Trp	Val	Phe	Val	Ile	Phe	His	Ala
		275					280					285			
Ile	Pro	Glu	Ile	His	Cys	Thr	Leu	Leu	Pro	Ala	Leu	Gln	Glu	Asn	Thr
		290				295					300				
Pro	Asn	Tyr	Phe	Asp	Thr	Ser	Gln	Pro	Arg	Met	Arg	Glu	Thr	Ala	Phe
305					310					315					320
Glu	Glu	Asp	Val	Gln	Leu	Pro	Arg	Ala	Tyr	Met	Glu	Asn	Lys	Ala	Phe
				325					330					335	
Ser	Met	Asp	Glu	His	Asn	Ala	Ala	Leu	Arg	Thr	Ala	Gly	Phe	Pro	Asn
			340					345					350		
Gly	Ser</														



<210> 122  
 <211> 1474  
 <212> DNA  
 <213> Homo sapiens

<400> 122  
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 caccaccacc aggtaattgg ccttatcagc tctgtgcctg tctccagtca ggctggaata 120  
 agtctcctca tatgtgcaag ctcgccctc ccctggaatc taaagcctcc tcagccttct 180  
 gagtcagcct gaaaggaaca ggccgaactg ctgtatgggc tctactgcca gtgtgacctc 240  
 accctctcca gtcacccctc ctgagttcca gctatgagtt cctgcaactt cacacatgcc 300  
 acctgtgtgc ttattgggtat cccaggatta gagaaagccc atttctgggt tggcttcccc 360  
 ctcctttcca tgtatgtagt ggcaatgtgt ggaaactgca tcgtggtcct catcgtaagg 420  
 acggaacgca gcctgcacgc tccgatgtac ctctttctct gcatgcttgc agccattgac 480  
 ctggccttat ccacatccac catgcctaag atccttgccc ttttctgggt tgattcccga 540  
 gagattagca ttgaggcctg tcttaccag atgttcttta ttcatgcctc ctcagccatt 600  
 gaatccacca tctgtctggc catggccttt gaccgttatg tggccatctg ccaccactg 660  
 cgccatgctg cagtgtcaa caatacagta acagcccaga ttggcatcgt ggctgtggtc 720  
 cgcggtatccc tctttttttt cccactgcct ctgctgatca agcggctggc cttctgccac 780  
 tccaatgtcc tctcgcactc ctattgtgtc caccaggatg taatgaagtt ggcctatgca 840  
 gacactttgc ccaatgtggt atatggtctt actgccattc tgctggatcat gggcgtggac 900  
 gtaatgttca tctccttgct ctattttctg ataatacгаа cggttctgca actgccttcc 960  
 aagtcagagc gggccaaggc ctttggaaac tgtgtgtcac acattggtgt ggtactcgcc 1020  
 ttctatgtgc cacttattgg cctctcagtt gtacaccgct ttggaacag cttcatccc 1080  
 attgtgcgtg ttgtcatggg tgacatctac ctgctgctgc ctctgtcat caatcccat 1140  
 atctatggtg ccaaaaccaa acagatcaga acacgggtgc tggctatggt caagatcagc 1200  
 tgtgacaagg acttgcaggc tgtgggaggc aagtgaccct taacactaca cttctcctta 1260  
 tctttattgg cttgataaac ataattattt ctaacactag cttatttcca gttgcccata 1320  
 agcacatcag tacttttctc tggctggaat agtaaactaa agtatggtac atctaccta 1380  
 aggactatta tgtggaataa tacatactaa tgaagtatta catgatttaa agactacaat 1440  
 aaaaccaaac atgcttataa cattaaaaaa aaaa 1474

<210> 123  
 <211> 320  
 <212> PRT  
 <213> Homo sapiens

<400> 123  
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 1 5 10 15  
 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
 20 25 30  
 Met Tyr Val Val Ala Met Cys Gly Asn Cys Ile Val Val Phe Ile Val  
 35 40 45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
 50 55 60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
 65 70 75 80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Ile Glu Ala Cys  
 85 90 95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
 100 105 110  
 Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
 115 120 125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly

134

130	135	140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu		
145	150	155
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser		160
	165	170
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu		175
	180	185
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val		190
	195	200
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val		205
	210	215
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys		220
225	230	235
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly		240
	245	250
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg		255
	260	265
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro		270
	275	280
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala		285
	290	295
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys		300
305	310	315
		320

&lt;210&gt; 124

&lt;211&gt; 2205

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 124

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acaactgggt ccgttaagcc cctctctcgc tcagacgcca tggagctgga tctgtctcca 240
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cccgggcccc ctgatacccc tctgcctgag gaggtaaaga ggtcccagcc tctcctcatc 360
ccaaccaccg gcaggaaact tcgagaggag gagaggcgtg ccacctccct cccctctatc 420
cccaaccctt tccctgagct ctgcagtcct ccctcacaga gcccaattct cgggggcccc 480
tccagtgaag gggggtgct ccccgcgat gccagccgcc cccatgtagt aaaggtgtac 540
agtgaggatg gggcctgcag gtctgtggag gtggcagcag gtgccacagc tcgccacgtg 600
tgtgaaatgc tgggtgcagcg agctcacgcc ttgagcgacg agacctgggg gctggtggag 660
tgccaccccc acctagcact ggagcggggt ttggaggacc acgagtccgt ggtggaagtg 720
caggctgcct ggcccggtgg cggagatagc cgcttcgtct tccggaaaaa cttcgccaag 780
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agctttcctg agatccaggg ctttctgcag ctgcggggtt caggacggaa gctttggaaa 960
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acccaactct gggtccacgg gcgcatttcc cgtgaggaga gccagcggct tattggacag 1560
cagggtctgg tagacggcct gttcctggtc cgggagagtc agcggaaccc ccagggtttt 1620

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135

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gtcctctctt tgtgccacct gcagaaagtg aagcattatc tcacacctgcc gagcgaggag 1680
gagggtcgcc tgtacttcag catggatgat ggccagaccc gcttactga cctgctgcag 1740
ctcgtggagt tccaccagct gaaccgcggc atcctgccgt gcttgctgcg ccattgctgc 1800
acgcggtgg ccctctgacc aggccgtgga ctggctcatg cctcagcccg ccttcaggct 1860
gcccgcgcc cctccacca tccagtggac tctggggcgc ggccacaggg gacgggatga 1920
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ccccctctcc ttctcctagc tctggaggtg ctgctctagg gcagggaatt atgggagaag 2100
tgggggcagc ccaggcggtt tcacgcccc cactttgtac agaccgagag gccagttgat 2160
ctgctctgtt ttatactagt gacaataaag attatttttt gatac 2205

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&lt;210&gt; 125

&lt;211&gt; 532

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

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Met Glu Leu Asp Leu Ser Pro Pro His Leu Ser Ser Ser Pro Glu Asp
1 5 10 15
Leu Trp Pro Ala Pro Gly Thr Pro Pro Gly Thr Pro Arg Pro Pro Asp
20 25 30
Thr Pro Leu Pro Glu Glu Val Lys Arg Ser Gln Pro Leu Leu Ile Pro
35 40 45
Thr Thr Gly Arg Lys Leu Arg Glu Glu Glu Arg Arg Ala Thr Ser Leu
50 55 60
Pro Ser Ile Pro Asn Pro Phe Pro Glu Leu Cys Ser Pro Pro Ser Gln
65 70 75 80
Ser Pro Ile Leu Gly Gly Pro Ser Ser Ala Arg Gly Leu Leu Pro Arg
85 90 95
Asp Ala Ser Arg Pro His Val Val Lys Val Tyr Ser Glu Asp Gly Ala
100 105 110
Cys Arg Ser Val Glu Val Ala Ala Gly Ala Thr Ala Arg His Val Cys
115 120 125
Glu Met Leu Val Gln Arg Ala His Ala Leu Ser Asp Glu Thr Trp Gly
130 135 140
Leu Val Glu Cys His Pro His Leu Ala Leu Glu Arg Gly Leu Glu Asp
145 150 155 160
His Glu Ser Val Val Glu Val Gln Ala Ala Trp Pro Val Gly Gly Asp
165 170 175
Ser Arg Phe Val Phe Arg Lys Asn Phe Ala Lys Tyr Glu Leu Phe Lys
180 185 190
Ser Ser Pro His Ser Leu Phe Pro Glu Lys Met Val Ser Ser Cys Leu
195 200 205
Asp Ala His Thr Gly Ile Ser His Glu Asp Leu Ile Gln Asn Phe Leu
210 215 220
Asn Ala Gly Ser Phe Pro Glu Ile Gln Gly Phe Leu Gln Leu Arg Gly
225 230 235 240
Ser Gly Arg Lys Leu Trp Lys Arg Phe Phe Cys Phe Leu Arg Arg Ser
245 250 255
Gly Leu Tyr Tyr Ser Thr Lys Gly Thr Ser Lys Asp Pro Arg His Leu
260 265 270
Gln Tyr Val Ala Asp Val Asn Glu Ser Asn Val Tyr Val Val Thr Gln
275 280 285
Gly Arg Lys Leu Tyr Gly Met Pro Thr Asp Phe Gly Phe Cys Val Lys
290 295 300
Pro Asn Lys Leu Arg Asn Gly His Lys Gly Leu Arg Ile Phe Cys Ser
305 310 315 320
Glu Asp Glu Gln Ser Arg Thr Cys Trp Leu Ala Ala Phe Arg Leu Phe

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<210> 126
<211> 1619
<212> DNA
<213> Homo sapiens
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<400> 126						
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gcccgcatt	ccctgtcctt	caccacgcgg	agctgccacc	ccctggagg	gtcttggggt	240
tctggaagaa	gcagccccc	actaggcgga	aatgggaagg	ccaccatgca	gaattctcaac	300
gaccgccttg	cctcctacct	ggagaaggtt	cgcgccctgg	aggaggccaa	catgaagctg	360
gaaagccgca	tcttgaaatg	gcaccagcag	agagatcctg	gcagtaagaa	agattattcc	420
cagtatgagg	aaaaacatcac	acacctgcag	gagcagatag	tggatggtaa	gatgaccaat	480
gctcagatta	ttcttctcat	tgacaatgcc	aggatggcag	tggatgactt	caacctcaag	540
tatgaaaatg	aacactcctt	taagaaagac	ttggaaattg	aagtcgaggg	cctccgaagg	600
accttagaca	acctgaccat	tgtcacaaca	gacctagaac	aggaggtgga	aggaatgagg	660
aaagagctca	ttctcatgaa	ggagcaccat	gagcaggaaa	tggaggagca	tcattgtcca	720
agtgacttca	atgtcaattg	gaaggtggat	acaggtccca	gggaagatct	gattaagggtc	780
ctggaggata	tgagaacaag	atatgagctt	ataataaaga	agaagcatcg	agacttggac	840
acttggtata	aagaacagtc	tgcagccatg	tccaggagg	gacccagtc	agccattgtg	900
cagagcagac	aaggtgacat	ccacgaactg	aagcgcacat	tccaggccct	ggagattgac	960
ctgcaggcac	agtacagcac	gaaatctgct	ttggaaaaca	tgttatccga	gaccagtcct	1020
cggtactcct	gcaagctcca	ggacatgcaa	gagatcatct	ccactatga	ggaggaactg	1080
acgcagctac	gccacgaact	ggagcggcag	aacaatgaat	accaagtgt	gctgggcatc	1140
aaaacccacc	tggagaagaa	aatcaccacg	taccgacggc	tcctcgagg	agagagtgaa	1200
gggacacggg	agaatacaga	gtcgagcatg	aaagtgtctg	caactccaaa	gatcaaggcc	1260
ataacccagg	agaccatcaa	cgggaagatta	gttctttgtc	aagtgaatga	aatccaaaag	1320
cacgcattag	accaatgaaa	gtttccgcct	gttgtaaagt	ctattttccc	ccaaggaaaag	1380

137

tccttgcaca gacaccagt agtgagttct aaaagatacc cttggaatta tcagactcag 1440  
 aaacttttat tttttttttt ctgtaacagt ctcaccagac ttctcataat gctcttaata 1500  
 tattgcactt ttctaataca agtgcgagtt tatgagggta aagctctact ttcctactgc 1560  
 agccttcaga ttctcatcat tttgcatcta tttttagacc aataaaaactc cgcactagc 1619

&lt;210&gt; 127

&lt;211&gt; 422

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

Met	Asn	Ser	Gly	His	Ser	Phe	Ser	Gln	Thr	Pro	Ser	Ala	Ser	Phe	His
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Gly	Ala	Gly	Gly	Gly	Trp	Gly	Arg	Pro	Arg	Ser	Phe	Pro	Arg	Ala	Pro
		20						25					30		
Thr	Val	His	Gly	Gly	Ala	Gly	Gly	Ala	Arg	Ile	Ser	Leu	Ser	Phe	Thr
		35					40					45			
Thr	Arg	Ser	Cys	Pro	Pro	Pro	Gly	Gly	Ser	Trp	Gly	Ser	Gly	Arg	Ser
	50					55					60				
Ser	Pro	Leu	Leu	Gly	Gly	Asn	Gly	Lys	Ala	Thr	Met	Gln	Asn	Leu	Asn
65				70					75					80	
Asp	Arg	Leu	Ala	Ser	Tyr	Leu	Glu	Lys	Val	Arg	Ala	Leu	Glu	Glu	Ala
			85					90					95		
Asn	Met	Lys	Leu	Glu	Ser	Arg	Ile	Leu	Lys	Trp	His	Gln	Gln	Arg	Asp
		100						105					110		
Pro	Gly	Ser	Lys	Lys	Asp	Tyr	Ser	Gln	Tyr	Glu	Glu	Asn	Ile	Thr	His
	115						120					125			
Leu	Gln	Glu	Gln	Ile	Val	Asp	Gly	Lys	Met	Thr	Asn	Ala	Gln	Ile	Ile
	130					135					140				
Leu	Leu	Ile	Asp	Asn	Ala	Arg	Met	Ala	Val	Asp	Asp	Phe	Asn	Leu	Lys
145				150					155					160	
Tyr	Glu	Asn	Glu	His	Ser	Phe	Lys	Lys	Asp	Leu	Glu	Ile	Glu	Val	Glu
			165					170					175		
Gly	Leu	Arg	Arg	Thr	Leu	Asp	Asn	Leu	Thr	Ile	Val	Thr	Thr	Asp	Leu
		180					185						190		
Glu	Gln	Glu	Val	Glu	Gly	Met	Arg	Lys	Glu	Leu	Ile	Leu	Met	Lys	Glu
	195					200						205			
His	His	Glu	Gln	Glu	Met	Glu	Glu	His	His	Val	Pro	Ser	Asp	Phe	Asn
	210					215					220				
Val	Asn	Val	Lys	Val	Asp	Thr	Gly	Pro	Arg	Glu	Asp	Leu	Ile	Lys	Val
225				230					235					240	
Leu	Glu	Asp	Met	Arg	Gln	Glu	Tyr	Glu	Leu	Ile	Ile	Lys	Lys	Lys	His
			245					250					255		
Arg	Asp	Leu	Asp	Thr	Trp	Tyr	Lys	Glu	Gln	Ser	Ala	Ala	Met	Ser	Gln
		260					265						270		
Glu	Ala	Ala	Ser	Pro	Ala	Thr	Val	Gln	Ser	Arg	Gln	Gly	Asp	Ile	His
	275						280					285			
Glu	Leu	Lys	Arg	Thr	Phe	Gln	Ala	Leu	Glu	Ile	Asp	Leu	Gln	Ala	Gln
	290					295					300				
Tyr	Ser	Thr	Lys	Ser	Ala	Leu	Glu	Asn	Met	Leu	Ser	Glu	Thr	Gln	Ser
305				310					315					320	
Arg	Tyr	Ser	Cys	Lys	Leu	Gln	Asp	Met	Gln	Glu	Ile	Ile	Ser	His	Tyr
			325					330					335		
Glu	Glu	Glu	Leu	Thr	Gln	Leu	Arg	His	Glu	Leu	Glu	Arg	Gln	Asn	Asn
		340					345					350			
Glu	Tyr	Gln	Val	Leu	Leu	Gly	Ile	Lys	Thr	His	Leu	Glu	Lys	Glu	Ile
	355					360					365				
Thr	Thr	Tyr	Arg	Arg	Leu	Leu	Glu	Gly	Glu	Ser	Glu	Gly	Thr	Arg	Glu

138

370                                      375                                      380  
 Glu Ser Lys Ser Ser Met Lys Val Ser Ala Thr Pro Lys Ile Lys Ala  
 385                                      390                                      395                                      400  
 Ile Thr Gln Glu Thr Ile Asn Gly Arg Leu Val Leu Cys Gln Val Asn  
                                     405                                      410                                      415  
 Glu Ile Gln Lys His Ala  
                                     420

<210> 128  
 <211> 1359  
 <212> DNA  
 <213> Homo sapiens

<400> 128  
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 cactaaaacg tccctgccta caaatcatcc ggccaaatta tgagttcatt gtattatgcg 120  
 aatgctttat tttctaaata tccagcctca agttcggttt tcgctaccgg agccttceca 180  
 gaacaaactt cttgtgcgtt tgctccaac cccagcgcc cgggctatgg agcgggttcg 240  
 ggcgcttcct tcgccgctc gatgcaggc ttgtaacccg gcgggggggg catggcgggc 300  
 cagagcgcg cggcggtcta cgcgccggc tatgggctcg agccgagttc cttcaacatg 360  
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 gcgggcgcca aggagcagag ggactcggac ttggcggccg agagtaactt ccgatctac 480  
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 <211> 217  
 <212> PRT  
 <213> Homo sapiens

<400> 129  
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 1                                      5                                      10                                      15  
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                                     20                                      25                                      30  
 Ala Phe Ala Ser Asn Pro Gln Arg Pro Gly Tyr Gly Ala Gly Ser Gly  
                                     35                                      40                                      45  
 Ala Ser Phe Ala Gly Ser Met Gln Gly Leu Tyr Pro Gly Gly Gly Gly  
                                     50                                      55                                      60  
 Met Ala Gly Gln Ser Ala Ala Gly Val Tyr Ala Ala Gly Tyr Gly Leu  
 65                                      70                                      75                                      80  
 Glu Pro Ser Ser Phe Asn Met His Cys Ala Pro Phe Glu Gln Asn Leu  
                                     85                                      90                                      95  
 Ser Gly Val Cys Pro Gly Asp Ser Ala Lys Ala Ala Gly Ala Lys Glu

139

100	105	110
Gln Arg Asp Ser Asp Leu Ala Ala Glu Ser Asn Phe Arg Ile Tyr Pro		
115	120	125
Ser Met Arg Ser Ser Gly Thr Asp Arg Lys Arg Gly Arg Gln Thr Tyr		
130	135	140
Thr Arg Tyr Gln Thr Leu Glu Leu Glu Lys Glu Phe His Tyr Asn Arg		
145	150	155
Tyr Leu Thr Arg Arg Arg Arg Ile Glu Ile Ala His Ala Leu Cys Leu		
165	170	175
Thr Glu Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp		
180	185	190
Lys Lys Glu Asn Lys Thr Ala Gly Pro Gly Thr Thr Gly Gln Asp Arg		
195	200	205
Ala Glu Ala Glu Glu Glu Glu Glu Glu		
210	215	

&lt;210&gt; 130

&lt;211&gt; 1257

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

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&lt;210&gt; 131

&lt;211&gt; 278

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

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Val Pro Leu Leu Gly Leu Leu Arg Leu Gln Leu Arg Ala Ala Arg Gln		
20	25	30
Pro Gly Ala Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu		
35	40	45
Arg Gly Leu Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser		

140

50	55	60
Ala Ser Glu Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg		
65	70	75
Glu Val Val Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly		80
	85	90
Val Pro Gly Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr		95
	100	105
Pro Gly Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys		110
	115	120
Leu Arg Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys		125
	130	135
Ser Trp Ser Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu		140
	145	150
Cys Thr Phe Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe		155
	160	165
Ser Gly Ser Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp		170
	175	180
Tyr Phe Thr Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu		185
	190	195
Ala Ile Ile Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile		200
	205	210
Asn Ile His Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly		215
	220	225
Ala Gly Leu Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr		230
	235	240
Pro Lys Gly Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile		245
	250	255
Ile Glu Glu Leu Pro Lys		260
	265	270
	275	

&lt;210&gt; 132

&lt;211&gt; 1177

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

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aaaattattt	ccaacaaccw	waaaaaaaaa	aaaaagg			1177



141

<210> 133  
 <211> 210  
 <212> PRT  
 <213> Homo sapiens

<400> 133  
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 Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile Pro  
 35 40 45  
 Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu Ser  
 50 55 60  
 Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser Ser  
 65 70 75 80  
 Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe Thr  
 85 90 95  
 Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser Leu  
 100 105 110  
 Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr Phe  
 115 120 125  
 Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile Tyr  
 130 135 140  
 Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His Arg  
 145 150 155 160  
 Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu Val  
 165 170 175  
 Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly Asp  
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 Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu Leu  
 195 200 205  
 Pro Lys  
 210

<210> 134  
 <211> 1340  
 <212> DNA  
 <213> Homo sapiens

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142

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&lt;210&gt; 135

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 135

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Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser Ala Ser Glu
      20          25          30
Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg Glu Val Val
      35          40          45
Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro Gly
      50          55          60
Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile
      65          70          75          80
Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu
      85          90          95
Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser
      100          105          110
Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe
      115          120          125
Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser
      130          135          140
Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr
      145          150          155          160
Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile
      165          170          175
Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His
      180          185          190
Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu
      195          200          205
Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly
      210          215          220
Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu
      225          230          235          240
Leu Pro Lys

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&lt;210&gt; 136

&lt;211&gt; 5519

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 136

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&lt;210&gt; 137

&lt;211&gt; 765

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 137

```

Met Ala Gly Phe Lys Arg Gly Tyr Asp Gly Lys Ile Ala Gly Leu Tyr
 1          5          10          15
Asp Leu Asp Lys Thr Leu Gly Arg Gly His Phe Ala Val Val Lys Leu
 20          25          30
Ala Arg His Val Phe Thr Gly Glu Lys Val Ala Val Lys Val Ile Asp
 35          40          45
Lys Thr Lys Leu Asp Thr Leu Ala Thr Gly His Leu Phe Gln Glu Val
 50          55          60
Arg Cys Met Lys Leu Val Gln His Pro Asn Ile Val Arg Leu Tyr Glu
 65          70          75          80
Val Ile Asp Thr Gln Thr Lys Leu Tyr Leu Ile Leu Glu Leu Gly Asp
 85          90          95
Glu Gly Asp Met Phe Asp Tyr Ile Met Lys His Glu Glu Gly Leu Asn
100          105          110
Glu Asp Leu Pro Lys Lys Tyr Phe Ala Gln Ile Val His Ala Ile Ser
115          120          125
Tyr Cys His Lys Leu His Val Val His Arg Asp Leu Lys Pro Glu Asn
130          135          140
Val Val Phe Phe Glu Lys Gln Gly Leu Val Lys Leu Thr Asp Phe Gly
145          150          155          160
Phe Ser Asn Lys Phe Gln Pro Gly Lys Lys Leu Thr Thr Ser Cys Gly

```

[illegible]

146

625					630					635					640	
Gly	Glu	Leu	Val	Glu	Ser	Leu	Lys	Leu	Met	Ser	Leu	Cys	Leu	Gly	Ser	
				645						650				655		
Gln	Leu	His	Gly	Ser	Thr	Lys	Tyr	Ile	Ile	Asp	Pro	Gln	Asn	Gly	Leu	
			660					665					670			
Ser	Phe	Ser	Ser	Val	Lys	Val	Gln	Glu	Lys	Ser	Thr	Trp	Lys	Met	Cys	
		675						680					685			
Ile	Ser	Ser	Thr	Gly	Asn	Ala	Gly	Gln	Val	Pro	Ala	Val	Gly	Gly	Ile	
	690					695					700					
Lys	Phe	Phe	Ser	Asp	His	Met	Ala	Asp	Thr	Thr	Thr	Glu	Leu	Glu	Arg	
705					710					715					720	
Ile	Lys	Ser	Lys	Asn	Leu	Lys	Asn	Asn	Val	Leu	Gln	Leu	Pro	Leu	Cys	
				725				730					735			
Glu	Lys	Thr	Ile	Ser	Val	Asn	Ile	Gln	Arg	Asn	Pro	Lys	Glu	Gly	Leu	
			740					745					750			
Leu	Cys	Ala	Ser	Ser	Pro	Ala	Ser	Cys	Cys	His	Val	Ile				
	755					760					765					

&lt;210&gt; 138

&lt;211&gt; 2029

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

gagaagagag	tcgaggacct	ccatgtaggt	gccacggtgg	ccccagcag	cagaagggac	60
tttacctttg	acctctacag	ggccttggt	tccgctgccc	ccagccagaa	catcttcttc	120
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aagatgcaga	tcctggaggg	cctgggcctc	aacctccaga	aaagctcaga	gaaggagctg	240
cacagaggct	ttcagcagct	ccttcaggaa	ctcaaccagc	ccagagatgg	cttcagctg	300
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cattcatcct	ttaagaaaaa	catctggata	tcaaggtgga	aatggcccat	ttaatgattg	1860
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gaagcctttt	gcaaatagta	gagtgtcagt	tgcagggtgcc	aatgactaac	tttttgaatt	1980

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2029

<210> 139

<211> 379

<212> PRT

<213> Homo sapiens

<400> 139

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Ser	Arg	Arg	Asp 20	Phe	Thr	Phe	Asp 25	Leu	Tyr	Arg	Ala	Leu	Ala 30	Ser	Ala
Ala	Pro	Ser 35	Gln	Asn	Ile	Phe	Phe 40	Ser	Pro	Val	Ser	Ile 45	Ser	Met	Ser
Leu	Ala 50	Met	Leu	Ser	Leu	Gly 55	Ala	Gly	Ser	Ser	Thr 60	Lys	Met	Gln	Ile
Leu 65	Glu	Gly	Leu	Gly 70	Leu	Asn	Leu	Gln	Lys	Ser 75	Ser	Glu	Lys	Glu 80	Leu
His	Arg	Gly	Phe 85	Gln	Gln	Leu	Leu	Gln 90	Glu	Leu	Asn	Gln 95	Pro	Arg	Asp
Gly	Phe	Gln 100	Leu	Ser	Leu	Gly	Asn 105	Ala	Leu	Phe	Thr	Asp 110	Leu	Val	Val
Asp	Leu	Gln 115	Asp	Thr	Phe	Val	Ser 120	Ala	Met	Lys	Thr 125	Leu	Tyr	Leu	Ala
Asp	Thr 130	Phe	Pro	Thr	Asn	Phe 135	Arg	Asp	Ser	Ala	Gly 140	Ala	Met	Lys	Gln
Ile 145	Asn	Asp	Tyr	Val 150	Ala	Lys	Gln	Thr	Lys	Gly 155	Lys	Ile	Val	Asp	Leu 160
Leu	Lys	Asn 165	Leu	Asp	Ser	Asn	Ala	Val 170	Val	Ile	Met	Val 175	Asn	Tyr	Ile
Phe	Phe	Lys 180	Ala	Lys	Trp	Glu	Thr 185	Ser	Phe	Asn	His	Lys 190	Gly	Thr	Gln
Glu	Gln	Asp 195	Phe	Tyr	Val	Thr	Ser 200	Glu	Thr	Val	Val 205	Arg	Val	Pro	Met
Met	Ser 210	Arg	Glu	Asp	Gln	Tyr	His 215	Tyr	Leu	Leu	Asp 220	Arg	Asn	Leu	Ser
Cys 225	Arg	Val	Val	Gly 230	Val	Pro	Tyr	Gln	Gly	Asn 235	Ala	Thr	Ala	Leu	Phe 240
Ile	Leu	Pro	Ser 245	Glu	Gly	Lys	Met	Gln 250	Gln	Val	Glu	Asn	Gly 255	Leu	Ser
Glu	Lys	Thr 260	Leu	Arg	Lys	Trp	Leu	Lys 265	Met	Phe	Lys	Lys 270	Arg	Gln	Leu
Glu	Leu	Tyr 275	Leu	Pro	Lys	Phe	Ser 280	Ile	Glu	Gly	Ser	Tyr 285	Gln	Leu	Glu
Lys	Val 290	Leu	Pro	Ser	Leu	Gly 295	Ile	Ser	Asn	Val	Phe 300	Thr	Ser	His	Ala
Asp 305	Leu	Ser	Gly	Ile 310	Ser	Asn	His	Ser	Asn	Ile 315	Gln	Val	Ser	Glu	Met 320
Val	His	Lys	Ala 325	Val	Val	Glu	Val	Asp 330	Glu	Ser	Gly	Thr 335	Arg	Ala	Ala
Ala	Ala	Thr 340	Gly	Thr	Ile	Phe	Thr 345	Phe	Arg	Ser	Ala	Arg 350	Leu	Asn	Ser
Gln	Arg	Leu 355	Val	Phe	Asn	Arg	Pro 360	Phe	Leu	Met	Phe	Ile 365	Val	Asp	Asn
Asn	Ile 370	Leu	Phe	Leu	Gly	Lys 375	Val	Asn	Arg	Pro					

148

<210> 140  
 <211> 2058  
 <212> DNA  
 <213> Homo sapiens

<400> 140

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tcacattcac tttaaatttt tctgtatata gaaaggaaaa ctagcctggg caacatgatg 2040
aaaccccatc tccactgc
2058

```

<210> 141  
 <211> 413  
 <212> PRT  
 <213> Homo sapiens

<400> 141

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Met Val Glu Arg Cys Ser Arg Gln Gly Cys Thr Ile Thr Met Ala Tyr
1           5           10           15
Ile Asp Tyr Asn Met Ile Val Ala Phe Met Leu Gly Asn Tyr Ile Asn
20           25           30
Leu Arg Glu Ser Ser Thr Glu Pro Asn Asp Ser Leu Trp Phe Ser Leu
35           40           45
Gln Lys Lys Asn Asp Thr Thr Glu Ile Glu Thr Leu Leu Leu Asn Thr
50           55           60
Ala Pro Lys Ile Ile Asp Glu Gln Leu Val Cys Arg Leu Ser Lys Thr
65           70           75           80

```



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<210> 142
<211> 1032
<212> DNA
<213> Homo sapiens
```

<400> 142						
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gctggacgtc	cccacggcgg	cggtgcaggc	gtccctctg	caagcgttag	acttctttgg	180
gaatggggca	ccagttaact	acaagacagg	caatctatac	ctgcgggggc	ccctgaagaa	240
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cacgtcggtg	ccctacggaa	acgcacagga	acaaaatgtc	agtgccaggt	gggagttcaa	420
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150

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cagatgtctt ccagccaccg cagcagtatg tgcctgggt caccgtcaat gggaaaccct 720
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aactagttta at 1032

```

&lt;210&gt; 143

&lt;211&gt; 303

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 143

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Met Asp Ser Arg His Thr Phe Ala Pro Ala Ala Met Thr Leu Ser Pro
1      5      10      15
Leu Leu Leu Phe Leu Pro Pro Leu Leu Leu Leu Asp Val Pro Thr
20      25      30
Ala Ala Val Gln Ala Ser Pro Leu Gln Ala Leu Asp Phe Phe Gly Asn
35      40      45
Gly Pro Pro Val Asn Tyr Lys Thr Gly Asn Leu Tyr Leu Arg Gly Pro
50      55      60
Leu Lys Lys Ser Asn Ala Pro Leu Val Asn Val Thr Leu Tyr Tyr Glu
65      70      75      80
Ala Leu Cys Gly Gly Cys Arg Ala Phe Leu Ile Arg Glu Leu Phe Pro
85      90      95
Thr Trp Leu Leu Val Met Glu Ile Leu Asn Val Thr Ser Val Pro Tyr
100     105     110
Gly Asn Ala Gln Glu Gln Asn Val Ser Gly Arg Trp Glu Phe Lys Cys
115     120     125
Gln Leu Gly Glu Glu Glu Cys Lys Phe Asn Lys Val Glu Ala Cys Val
130     135     140
Leu Asp Glu Leu Asp Met Glu Leu Ala Phe Leu Thr Met Ser Gly Met
145     150     155     160
Ala Trp Lys Ser Leu Arg Thr Trp Arg Glu Val Cys His Tyr Ala Cys
165     170     175
Ser Ser Thr Pro Gln Gly Cys Arg Gln Asn Tyr His Gly Val Cys Asn
180     185     190
Gly Gly Pro Arg His Ala Ala His Ala Arg Gln Arg Pro Ala Asp Arg
195     200     205
Cys Ser Pro Ala Thr Ala Arg Val Cys Ala Leu Gly His Arg Gln Trp
210     215     220
Glu Thr Leu Gly Arg Ser Asp Pro Ala Pro Tyr Pro Cys Leu Pro Val
225     230     235     240
Val Pro Gly Gln Glu Ala Gly Cys Leu Pro Phe Leu Asn Gln Leu Pro
245     250     255
Pro Glu Cys Leu Leu Arg Val Leu Ala Gly Gly Leu Arg Arg Ala His
260     265     270
Gly Arg Arg Val Gly Thr Arg Leu Pro Ala Phe Phe Ser Asp Pro Asp
275     280     285
Pro Arg His Leu Leu Leu Thr Asn Trp Lys Ile Leu Cys Ile Pro
290     295     300

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&lt;210&gt; 144

&lt;211&gt; 1356

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 144

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cagacgaatt ctcccccccc ccccaaaaaa aaaagccatc cccccgctct gccccgtcgc 420
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ccaacgcccg ctgttcggtt tgcgacacgc agcagggagg tggcgggcag cgtcgccggc 540
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ctggtggaca ccctccagtt cgtctgtggg gaccgcggct tctacttcag caggccccga 720
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```

&lt;210&gt; 145

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 145

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Met Gly Ile Pro Met Gly Lys Ser Met Leu Val Leu Leu Thr Phe Leu
1          5          10          15
Ala Phe Ala Ser Cys Cys Ile Ala Ala Tyr Arg Pro Ser Glu Thr Leu
20          25          30
Cys Gly Gly Glu Leu Val Asp Thr Leu Gln Phe Val Cys Gly Asp Arg
35          40          45
Gly Phe Tyr Phe Ser Arg Pro Ala Ser Arg Val Ser Arg Arg Ser Arg
50          55          60
Gly Ile Val Glu Glu Cys Cys Phe Arg Ser Cys Asp Leu Ala Leu Leu
65          70          75          80
Glu Thr Tyr Cys Ala Thr Pro Ala Lys Ser Glu Arg Asp Val Ser Thr
85          90          95
Pro Pro Thr Val Leu Pro Asp Asn Phe Pro Arg Tyr Pro Val Gly Lys
100         105         110
Phe Phe Gln Tyr Asp Thr Trp Lys Gln Ser Thr Gln Arg Leu Arg Arg
115         120         125
Gly Leu Pro Ala Leu Leu Arg Ala Arg Arg Gly His Val Leu Ala Lys
130         135         140
Glu Leu Glu Ala Phe Arg Glu Ala Lys Arg His Arg Pro Leu Ile Ala
145         150         155         160
Leu Pro Thr Gln Asp Pro Ala His Gly Gly Ala Pro Pro Glu Met Ala
165         170         175
Ser Asn Arg Lys

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180

<210> 146  
 <211> 3667  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 146

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aaaaaaa 3667

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&lt;210&gt; 147

&lt;211&gt; 556

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

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Met Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Pro Ala Val Thr Ala
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Asp Asp Leu Arg Gln Leu Phe Gly Asp Arg Lys Leu Pro Leu Ala Gly
      20          25          30
Gln Val Leu Leu Lys Ser Gly Tyr Ala Phe Val Asp Tyr Pro Asp Gln
      35          40          45
Asn Trp Ala Ile Arg Ala Ile Glu Thr Leu Ser Gly Lys Val Glu Leu
      50          55          60
His Gly Lys Ile Met Glu Val Asp Tyr Ser Val Ser Lys Lys Leu Arg
      65          70          75          80
Ser Arg Lys Ile Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu
      85          90          95
Val Leu Asp Gly Leu Leu Ala Gln Tyr Gly Thr Val Glu Asn Val Glu
      100          105          110
Gln Val Asn Thr Asp Thr Glu Thr Ala Val Val Asn Val Thr Tyr Ala
      115          120          125
Thr Arg Glu Glu Ala Lys Ile Ala Met Glu Lys Leu Ser Gly His Gln
      130          135          140
Phe Glu Asn Tyr Ser Phe Lys Ile Ser Tyr Ile Pro Asp Glu Glu Val
      145          150          155          160
Ser Ser Pro Ser Pro Pro Gln Arg Ala Gln Arg Gly Asp His Ser Ser
      165          170          175
Arg Glu Gln Gly His Ala Pro Gly Gly Thr Ser Gln Ala Arg Gln Ile
      180          185          190
Asp Phe Pro Leu Arg Ile Leu Val Pro Thr Gln Phe Val Gly Ala Ile
      195          200          205
Ile Gly Lys Glu Gly Leu Thr Ile Lys Asn Ile Thr Lys Gln Thr Gln
      210          215          220
Ser Arg Val Asp Ile His Arg Lys Glu Asn Ser Gly Ala Ala Glu Lys
      225          230          235          240
Pro Val Thr Ile His Ala Thr Pro Glu Gly Thr Ser Glu Ala Cys Arg
      245          250          255
Met Ile Leu Glu Ile Met Gln Lys Glu Ala Asp Glu Thr Lys Leu Ala
      260          265          270
Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Gly Leu Val Gly Arg
      275          280          285
Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu His Glu Thr
      290          295          300

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154

Gly Thr Lys Ile Thr Ile Ser Ser Leu Gln Asp Leu Ser Ile Tyr Asn  
 305 310 315 320  
 Pro Glu Arg Thr Ile Thr Val Lys Gly Thr Val Glu Ala Cys Ala Ser  
 325 330 335  
 Ala Glu Ile Glu Ile Met Lys Lys Leu Arg Glu Ala Phe Glu Asn Asp  
 340 345 350  
 Met Leu Ala Val Asn Thr His Ser Gly Tyr Phe Ser Ser Leu Tyr Pro  
 355 360 365  
 His His Gln Phe Gly Pro Phe Pro His His His Ser Tyr Pro Glu Gln  
 370 375 380  
 Glu Ile Val Asn Leu Phe Ile Pro Thr Gln Ala Val Gly Ala Ile Ile  
 385 390 395 400  
 Gly Lys Lys Gly Ala His Ile Lys Gln Leu Ala Arg Phe Ala Gly Ala  
 405 410 415  
 Ser Ile Lys Ile Ala Pro Ala Glu Gly Pro Asp Val Ser Glu Arg Met  
 420 425 430  
 Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe Lys Ala Gln Gly Arg  
 435 440 445  
 Ile Phe Gly Lys Leu Lys Glu Glu Asn Phe Phe Asn Pro Lys Glu Glu  
 450 455 460  
 Val Lys Leu Glu Ala His Ile Arg Val Pro Ser Ser Thr Ala Gly Arg  
 465 470 475 480  
 Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu Leu Gln Asn Leu Thr  
 485 490 495  
 Ser Ala Glu Val Ile Val Pro Arg Asp Gln Thr Pro Asp Glu Asn Glu  
 500 505 510  
 Glu Val Ile Val Arg Ile Ile Gly His Phe Phe Ala Ser Gln Thr Ala  
 515 520 525  
 Gln Arg Lys Ile Arg Glu Ile Val Gln Gln Val Lys Gln Gln Glu Gln  
 530 535 540  
 Lys Tyr Pro Gln Gly Val Ala Ser Gln Arg Ser Lys  
 545 550 555

&lt;210&gt; 148

&lt;211&gt; 1475

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

cccagaggag cagactacaa gaatggcaca cgctatggaa aactcctgga caatcagtaa 60  
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 ccagcttcga gaaagagttg agaagttaaa catgctcagc attgatcatc tcacagacca 240  
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155

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&lt;210&gt; 149

&lt;211&gt; 403

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 149

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Met Ala His Ala Met Glu Asn Ser Trp Thr Ile Ser Lys Glu Tyr His
1      5      10      15
Ile Asp Glu Glu Val Gly Phe Ala Leu Pro Asn Pro Gln Glu Asn Leu
20     25     30
Pro Asp Phe Tyr Asn Asp Trp Met Phe Ile Ala Lys His Leu Pro Asp
35     40     45
Leu Ile Glu Ser Gly Gln Leu Arg Glu Arg Val Glu Lys Leu Asn Met
50     55     60
Leu Ser Ile Asp His Leu Thr Asp His Lys Ser Gln Arg Leu Ala Arg
65     70     75     80
Leu Val Leu Gly Cys Ile Thr Met Ala Tyr Val Trp Gly Lys Gly His
85     90     95
Gly Asp Val Arg Lys Val Leu Pro Arg Asn Ile Ala Val Pro Tyr Cys
100    105    110
Gln Leu Ser Lys Lys Leu Glu Leu Pro Pro Ile Leu Val Tyr Ala Asp
115    120    125
Cys Val Leu Ala Asn Trp Lys Lys Lys Asp Pro Asn Lys Pro Leu Thr
130    135    140
Tyr Glu Asn Met Asp Val Leu Phe Ser Phe Arg Asp Gly Asp Cys Ser
145    150    155    160
Lys Gly Phe Phe Leu Val Ser Leu Leu Val Glu Ile Ala Ala Ala Ser
165    170    175
Ala Ile Lys Val Ile Pro Thr Val Phe Lys Ala Met Gln Met Gln Glu
180    185    190
Arg Asp Thr Leu Leu Lys Ala Leu Leu Glu Ile Ala Ser Cys Leu Glu
195    200    205
Lys Ala Leu Gln Val Phe His Gln Ile His Asp His Val Asn Pro Lys
210    215    220
Ala Phe Phe Ser Val Leu Arg Ile Tyr Leu Ser Gly Trp Lys Gly Asn
225    230    235    240
Pro Gln Leu Ser Asp Gly Leu Val Tyr Glu Gly Phe Trp Glu Asp Pro
245    250    255
Lys Glu Phe Ala Gly Gly Ser Ala Gly Gln Ser Ser Val Phe Gln Cys
260    265    270
Phe Asp Val Leu Leu Gly Ile Gln Gln Thr Ala Gly Gly Gly His Ala
275    280    285
Ala Gln Phe Leu Gln Asp Met Arg Arg Tyr Met Pro Pro Ala His Arg
290    295    300
Asn Phe Leu Cys Ser Leu Glu Ser Asn Pro Ser Val Arg Glu Phe Val
305    310    315    320
Leu Ser Lys Gly Asp Ala Gly Leu Arg Glu Ala Tyr Asp Ala Cys Val
325    330    335
Lys Ala Leu Val Ser Leu Arg Ser Tyr His Leu Gln Ile Val Thr Lys
340    345    350

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156

Tyr Ile Leu Ile Pro Ala Ser Gln Gln Pro Lys Glu Asn Lys Thr Ser  
 355 360 365  
 Glu Asp Pro Ser Lys Leu Glu Ala Lys Gly Thr Gly Gly Thr Asp Leu  
 370 375 380  
 Met Asn Phe Leu Lys Thr Val Arg Ser Thr Thr Glu Lys Ser Leu Leu  
 385 390 395 400  
 Lys Glu Gly

<210> 150  
 <211> 2129  
 <212> DNA  
 <213> Homo sapiens

<400> 150  
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 aatccacgct ggcgttgacg ctaggccagc ggctcggcgg tgagatcgtc agcgctgact 180  
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 aatttaaaaa aaaaaaaaaa aaaaaaaaaa 2129

<210> 151  
 <211> 465  
 <212> PRT  
 <213> Homo sapiens



157

&lt;400&gt; 151

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Met Ala Ser Val Ala Ala Ala Arg Ala Val Pro Val Gly Ser Gly Leu
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Arg Gly Leu Gln Arg Thr Leu Pro Leu Val Val Ile Leu Gly Ala Thr
 20          25          30
Gly Thr Ser Thr Leu Ala Leu Gln Leu Gly Gln Arg Leu Gly Gly Glu
 35          40          45
Ile Val Ser Ala Asp Ser Met Gln Val Tyr Glu Gly Leu Asp Ile Ile
 50          55          60
Thr Asn Lys Val Ser Ala Gln Glu Gln Arg Ile Cys Arg His His Met
 65          70          75          80
Ile Ser Phe Val Asp Pro Leu Val Thr Asn Tyr Thr Val Val Asp Phe
 85          90          95
Arg Asn Arg Ala Thr Ala Leu Ile Glu Asp Ile Phe Ala Arg Asp Lys
100          105          110
Ile Pro Ile Val Val Gly Gly Thr Asn Tyr Tyr Ile Glu Ser Leu Leu
115          120          125
Trp Lys Val Leu Val Asn Thr Lys Pro Gln Glu Met Gly Thr Glu Lys
130          135          140
Val Ile Asp Arg Lys Val Glu Leu Glu Lys Glu Asp Gly Leu Val Leu
145          150          155          160
His Lys Arg Leu Ser Gln Val Asp Pro Glu Met Ala Ala Lys Leu His
165          170          175
Pro His Asp Lys Arg Lys Val Ala Arg Ser Leu Gln Val Phe Glu Glu
180          185          190
Thr Gly Ile Ser His Ser Glu Phe Leu His Arg Gln His Thr Glu Glu
195          200          205
Gly Gly Gly Pro Leu Gly Gly Pro Leu Lys Phe Ser Asn Pro Cys Ile
210          215          220
Leu Trp Leu His Ala Asp Gln Ala Val Leu Asp Glu Arg Leu Asp Lys
225          230          235          240
Arg Val Asp Asp Met Leu Ala Ala Gly Leu Leu Glu Glu Leu Arg Asp
245          250          255
Phe His Arg Arg Tyr Asn Gln Lys Asn Val Ser Glu Asn Ser Gln Asp
260          265          270
Tyr Gln His Gly Ile Phe Gln Ser Ile Gly Phe Lys Glu Phe His Glu
275          280          285
Tyr Leu Ile Thr Glu Gly Lys Cys Thr Leu Glu Thr Ser Asn Gln Leu
290          295          300
Leu Lys Lys Gly Ile Glu Ala Leu Lys Gln Val Thr Lys Arg Tyr Ala
305          310          315          320
Arg Lys Gln Asn Arg Trp Val Lys Asn Arg Phe Leu Ser Arg Pro Gly
325          330          335
Pro Ile Val Pro Pro Val Tyr Gly Leu Glu Val Ser Asp Val Ser Lys
340          345          350
Trp Glu Glu Ser Val Leu Glu Pro Ala Leu Glu Ile Val Gln Ser Phe
355          360          365
Ile Gln Gly His Lys Pro Thr Ala Thr Pro Ile Lys Met Pro Tyr Asn
370          375          380
Glu Ala Glu Asn Lys Arg Ser Tyr His Leu Cys Asp Leu Cys Asp Arg
385          390          395          400
Ile Ile Ile Gly Asp Arg Glu Trp Ala Ala His Ile Lys Ser Lys Ser
405          410          415
His Leu Asn Gln Leu Lys Lys Arg Arg Arg Leu Asp Ser Asp Ala Val
420          425          430
Asn Thr Ile Glu Ser Gln Ser Val Ser Pro Asp His Asn Lys Glu Pro
435          440          445
Lys Glu Lys Gly Ser Pro Gly Gln Asn Asp Gln Glu Leu Lys Cys Ser

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158

450  
Val  
465

455

460

<210> 152  
<211> 2129  
<212> DNA  
<213> Homo sapiens

<400> 152  
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aatccacgct ggcgttgacg ctaggccagc ggctcggcgg tgagatcgtc agcgtgact 180  
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<213> Homo sapiens

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 Ala Val Asn Thr Ile Glu Ser Gln Ser Val Ser Pro Asp His Asn Lys  
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&lt;210&gt; 155

&lt;211&gt; 1066

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 155

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Gly Ser Leu Phe Gly Tyr Ser Val Ala Leu His Arg Gln Thr Glu Arg
50          55          60
Gln Gln Arg Tyr Leu Leu Leu Ala Gly Ala Pro Arg Glu Leu Ala Val
65          70          75          80
Pro Asp Gly Tyr Thr Asn Arg Thr Gly Ala Val Tyr Leu Cys Pro Leu
85          90          95
Thr Ala His Lys Asp Asp Cys Glu Arg Met Asn Ile Thr Val Lys Asn
100         105         110
Asp Pro Gly His His Ile Ile Glu Asp Met Trp Leu Gly Val Thr Val
115         120         125
Ala Ser Gln Gly Pro Ala Gly Arg Val Leu Val Cys Ala His Arg Tyr
130         135         140
Thr Gln Val Leu Trp Ser Gly Ser Glu Asp Gln Arg Arg Met Val Gly
145         150         155         160
Lys Cys Tyr Val Arg Gly Asn Asp Leu Glu Leu Asp Ser Ser Asp Asp
165         170         175
Trp Gln Thr Tyr His Asn Glu Met Cys Asn Ser Asn Thr Asp Tyr Leu
180         185         190
Glu Thr Gly Met Cys Gln Leu Gly Thr Ser Gly Gly Phe Thr Gln Asn
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Ser	Leu	Ser	Gly	Gln	Met	Asp	Val	Asp	Glu	Asn	Phe	Tyr	Pro	Asp	Leu
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Asp	Pro	Ala	Leu	Cys	Thr	Ala	Thr	Ser	Cys	Val	Gln	Val	Glu	Leu	Cys
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Thr	Leu	Ala	Tyr	Thr	Leu	Glu	Ala	Asp	Arg	Asp	Arg	Arg	Pro	Pro	Arg
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Leu	Arg	Phe	Ala	Gly	Ser	Glu	Ser	Ala	Val	Phe	His	Gly	Phe	Phe	Ser
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Leu	Arg	Asp	Lys	Leu	Arg	Pro	Ile	Ile	Ile	Ser	Met	Asn	Tyr	Ser	Leu
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Pro	Leu	Arg	Met	Pro	Asp	Arg	Pro	Arg	Leu	Gly	Leu	Arg	Ser	Leu	Asp
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163

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&lt;210&gt; 156

&lt;211&gt; 8747

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 156

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&lt;210&gt; 159

&lt;211&gt; 624

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 159

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20        25        30
Ser Glu Lys Thr His Pro Lys Asp Tyr Pro Arg Arg Ala Asn His Trp
35        40        45
Ser Ala Ile Ile Gly Gly Ser His Ser Lys Asn Tyr Val Leu Trp Glu
50        55        60
Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys Gln Val Ala Glu Leu Gly
65        70        75        80
Ser Pro Val Lys Met Glu Glu Glu Ile Arg Gln Gln Ser Asp Glu Val
85        90        95
Leu Thr Val Ile Lys Ala Lys Ala Gln Trp Pro Ala Trp Gln Pro Leu
100       105       110
Asn Val Arg Ala Ala Pro Ser Ala Glu Phe Ser Val Asp Arg Thr Arg
115       120       125
His Leu Met Ser Phe Leu Thr Met Met Gly Pro Ser Pro Asp Trp Asn

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170

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Val Gly Leu Ser Ala	Glu Asp Leu Cys Thr Lys	Glu Cys Gly Trp Val		
145	150	155	160	
Gln Lys Val Val Gln	Asp Leu Ile Pro Trp Asp	Ala Gly Thr Asp Ser		
	165	170	175	
Gly Val Thr Tyr Glu	Ser Pro Asn Lys Pro Thr	Ile Pro Gln Glu Lys		
	180	185	190	
Ile Arg Pro Leu Thr	Ser Leu Asp His Pro Gln	Ser Pro Phe Tyr Asp		
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Pro Glu Gly Gly Ser	Ile Thr Gln Val Ala Arg	Val Val Ile Glu Arg		
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Ile Ala Arg Lys Gly	Glu Gln Cys Asn Ile Val	Pro Asp Asn Val Asp		
225	230	235	240	
Asp Ile Val Ala Asp	Leu Ala Pro Glu Glu Lys	Asp Glu Asp Asp Thr		
	245	250	255	
Pro Glu Thr Cys Ile	Tyr Ser Asn Trp Ser Pro	Trp Ser Ala Cys Ser		
	260	265	270	
Ser Ser Thr Cys Asp	Lys Gly Lys Arg Met Arg	Gln Arg Met Leu Lys		
	275	280	285	
Ala Gln Leu Asp Leu	Ser Val Pro Cys Pro Asp	Thr Gln Asp Phe Gln		
	290	295	300	
Pro Cys Met Gly Pro	Gly Cys Ser Asp Glu Asp	Gly Ser Thr Cys Thr		
305	310	315	320	
Met Ser Glu Trp Ile	Thr Trp Ser Pro Cys Ser	Ile Ser Cys Gly Met		
	325	330	335	
Gly Met Arg Ser Arg	Glu Arg Tyr Val Lys Gln	Phe Pro Glu Asp Gly		
	340	345	350	
Ser Val Cys Thr Leu	Pro Thr Glu Glu Thr Glu	Lys Cys Thr Val Asn		
	355	360	365	
Glu Glu Cys Ser Pro	Ser Ser Cys Leu Met Thr	Glu Trp Gly Glu Trp		
	370	375	380	
Asp Glu Cys Ser Ala	Thr Cys Gly Met Gly Met	Lys Lys Arg His Arg		
385	390	395	400	
Met Ile Lys Met Asn	Pro Ala Asp Gly Ser Met	Cys Lys Ala Glu Thr		
	405	410	415	
Ser Gln Ala Glu Lys	Cys Met Met Pro Glu Cys	His Thr Ile Pro Cys		
	420	425	430	
Leu Leu Ser Pro Trp	Ser Glu Trp Ser Asp Cys	Ser Val Thr Cys Gly		
	435	440	445	
Lys Gly Met Arg Thr	Arg Gln Arg Met Leu Lys	Ser Leu Ala Glu Leu		
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Gly Asp Cys Asn Glu	Asp Leu Glu Gln Val Glu	Lys Cys Met Leu Pro		
465	470	475	480	
Glu Cys Pro Ile Asp	Cys Glu Leu Thr Glu Trp	Ser Gln Trp Ser Glu		
	485	490	495	
Cys Asn Lys Ser Cys	Gly Lys Gly His Val Ile	Arg Thr Arg Met Ile		
	500	505	510	
Gln Met Glu Pro Gln	Phe Gly Gly Ala Pro Cys	Pro Glu Thr Val Gln		
	515	520	525	
Arg Lys Lys Cys Arg	Ile Arg Lys Cys Leu Arg	Asn Pro Ser Ile Gln		
	530	535	540	
Lys Leu Arg Trp Arg	Glu Ala Arg Glu Ser Arg	Arg Ser Glu Gln Leu		
545	550	555	560	
Lys Glu Glu Ser Glu	Gly Glu Gln Phe Pro Gly	Cys Arg Met Arg Pro		
	565	570	575	
Trp Thr Ala Trp Ser	Glu Cys Thr Lys Leu Cys	Gly Gly Gly Ile Gln		
	580	585	590	
Glu Arg Tyr Met Thr	Val Lys Lys Arg Phe Lys	Ser Ser Gln Phe Thr		

	595		600		605										
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 <211> 3408  
 <212> DNA  
 <213> Homo sapiens

<400> 160  
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 ctctctggag agttcgagtt tcccgtctacc gaaacagtac ctggatgtga gctcccagac 180  
 agacatctcg ggaagcttcg gcatcaacag caacaatcag ttggcagaga aggtcagatt 240  
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 gcttgacagt gaggcctggc ctgggggtgct ggactcagag agggaccggc tgatccttat 360  
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 gggggaggtg gacagctgg agatggcccg gaagcggctg gaaaaggacc tgcaggcagc 480  
 ccgggacacc cagagcaagg cgctgacgga gaggttaaag ttaaacagta agaggaacca 540  
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 aagtctctca agcagcatgc agtccctgtc ctccagcagc agccccggat ccctcacgtc 660  
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 ccaggctgtg aacattgact gtggctaaag ttatttatgt ggtgttatat gaaggtactg 2760  
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172

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&lt;210&gt; 161

&lt;211&gt; 888

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

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20     25     30
Ser Asp Leu Trp Ser Ser Ser Ser Ser Leu Glu Ser Ser Ser Phe Pro
35     40     45
Leu Pro Lys Gln Tyr Leu Asp Val Ser Ser Gln Thr Asp Ile Ser Gly
50     55     60
Ser Phe Gly Ile Asn Ser Asn Asn Gln Leu Ala Glu Lys Val Arg Leu
65     70     75     80
Arg Leu Arg Tyr Glu Glu Ala Lys Arg Arg Ile Ala Asn Leu Lys Ile
85     90     95
Gln Leu Ala Lys Leu Asp Ser Glu Ala Trp Pro Gly Val Leu Asp Ser
100    105    110
Glu Arg Asp Arg Leu Ile Leu Ile Asn Glu Lys Glu Glu Leu Leu Lys
115    120    125
Glu Met Arg Phe Ile Ser Pro Arg Lys Trp Thr Gln Gly Glu Val Glu
130    135    140
Gln Leu Glu Met Ala Arg Lys Arg Leu Glu Lys Asp Leu Gln Ala Ala
145    150    155    160
Arg Asp Thr Gln Ser Lys Ala Leu Thr Glu Arg Leu Lys Leu Asn Ser
165    170    175
Lys Arg Asn Gln Leu Val Arg Glu Leu Glu Glu Ala Thr Arg Gln Val
180    185    190
Ala Thr Leu His Ser Gln Leu Lys Ser Leu Ser Ser Ser Met Gln Ser
195    200    205
Leu Ser Ser Gly Ser Ser Pro Gly Ser Leu Thr Ser Ser Arg Gly Ser
210    215    220
Leu Val Ala Ser Ser Leu Asp Ser Ser Thr Ser Ala Ser Phe Thr Asp
225    230    235    240
Leu Tyr Tyr Asp Pro Phe Glu Gln Leu Asp Ser Glu Leu Gln Ser Lys
245    250    255
Val Glu Phe Leu Leu Leu Glu Gly Ala Thr Gly Phe Arg Pro Ser Gly
260    265    270
Cys Ile Thr Thr Ile His Glu Asp Glu Val Ala Lys Thr Gln Lys Ala
275    280    285
Glu Gly Gly Gly Arg Leu Gln Ala Leu Arg Ser Leu Ser Gly Thr Pro
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Lys Ser Met Thr Ser Leu Ser Pro Arg Ser Ser Leu Ser Ser Pro Ser
305    310    315    320
Pro Pro Cys Ser Pro Leu Met Ala Asp Pro Leu Leu Ala Gly Asp Ala

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173

				325					330					.335			
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Cys	Glu	Leu	Ser	Leu	Gly	Asn	Ser	Ala	Gln	Glu	Arg	Tyr	Arg	Leu	Glu		
				355				360					365				
Glu	Pro	Gly	Thr	Glu	Gly	Lys	Gln	Leu	Gly	Gln	Ala	Val	Asn	Thr	Ala		
				370			375				380						
Gln	Gly	Cys	Gly	Leu	Lys	Val	Ala	Cys	Val	Ser	Ala	Ala	Val	Ser	Asp		
385					390					395					400		
Glu	Ser	Val	Ala	Gly	Asp	Ser	Gly	Val	Tyr	Glu	Ala	Ser	Val	Gln	Arg		
				405					410					415			
Leu	Gly	Ala	Ser	Glu	Ala	Ala	Ala	Phe	Asp	Ser	Asp	Glu	Ser	Glu	Ala		
				420				425					430				
Val	Gly	Ala	Thr	Arg	Ile	Gln	Ile	Ala	Leu	Lys	Tyr	Asp	Glu	Lys	Asn		
				435			440					445					
Lys	Gln	Phe	Ala	Ile	Leu	Ile	Ile	Gln	Leu	Ser	Asn	Leu	Ser	Ala	Leu		
	450					455				460							
Leu	Gln	Gln	Gln	Asp	Gln	Lys	Val	Asn	Ile	Arg	Val	Ala	Val	Leu	Pro		
465					470					475				480			
Cys	Ser	Glu	Ser	Thr	Cys	Leu	Phe	Arg	Thr	Arg	Pro	Leu	Asp	Ala			
				485				490					495				
Ser	Asp	Thr	Leu	Val	Phe	Asn	Glu	Val	Phe	Trp	Val	Ser	Met	Ser	Tyr		
				500				505					510				
Pro	Ala	Leu	His	Gln	Lys	Thr	Leu	Arg	Val	Asp	Val	Cys	Thr	Thr	Asp		
				515			520					525					
Arg	Ser	His	Leu	Glu	Glu	Cys	Leu	Gly	Gly	Ala	Gln	Ile	Ser	Leu	Ala		
	530					535				540							
Glu	Val	Cys	Arg	Ser	Gly	Glu	Arg	Ser	Thr	Arg	Trp	Tyr	Asn	Leu	Leu		
545					550					555					560		
Ser	Tyr	Lys	Tyr	Leu	Lys	Lys	Gln	Ser	Arg	Glu	Leu	Lys	Pro	Val	Gly		
				565				570					575				
Val	Met	Ala	Pro	Ala	Ser	Gly	Pro	Ala	Ser	Thr	Asp	Ala	Val	Ser	Ala		
				580				585					590				
Leu	Leu	Glu	Gln	Thr	Ala	Val	Glu	Leu	Glu	Lys	Arg	Gln	Glu	Gly	Arg		
				595			600					605					
Ser	Ser	Thr	Gln	Thr	Leu	Glu	Asp	Ser	Trp	Arg	Tyr	Glu	Glu	Thr	Ser		
	610					615					620						
Glu	Asn	Glu	Ala	Val	Ala	Glu	Glu	Glu	Glu	Glu	Glu	Val	Glu	Glu	Glu		
625					630					635					640		
Glu	Gly	Glu	Glu	Asp	Val	Phe	Thr	Glu	Lys	Ala	Ser	Pro	Asp	Met	Asp		
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Ala	Pro	Ser	Pro	Thr	Val	Val	Arg	Pro	Lys	Asp	Arg	Arg	Val	Gly	Thr		
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Pro	Ser	Gln	Gly	Pro	Phe	Leu	Arg	Gly	Ser	Thr	Ile	Ile	Arg	Ser	Lys		
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Thr	Phe	Ser	Pro	Gly	Pro	Gln	Ser	Gln	Tyr	Val	Cys	Arg	Leu	Asn	Arg		
705					710					715					720		
Ser	Asp	Ser	Asp	Ser	Ser	Thr	Leu	Ser	Lys	Lys	Pro	Pro	Phe	Val	Arg		
				725				730					735				
Asn	Ser	Leu	Glu	Arg	Arg	Ser	Val	Arg	Met	Lys	Arg	Pro	Ser	Ser	Val		
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Lys	Ser	Leu	Arg	Ser	Glu	Arg	Leu	Ile	Arg	Thr	Ser	Leu	Asp	Leu	Glu		
				755			760					765					
Leu	Asp	Leu	Gln	Ala	Thr	Arg	Thr	Trp	His	Ser	Gln	Leu	Thr	Gln	Glu		
	770					775					780						
Ile	Ser	Val	Leu	Lys	Glu	Leu	Lys	Glu	Gln	Leu	Glu	Gln	Ala	Lys	Ser		

174

785		790		795		800
His Gly Glu Lys	Glu Leu Pro Gln Trp	Leu Arg	Glu Asp Glu Arg Phe			
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Arg Leu Leu Leu	Arg Met Leu Glu	Lys Arg Met	Asp Arg Ala Glu His			
	820		825			830
Lys Gly Glu Leu	Gln Thr Asp Lys	Met Met Arg	Ala Ala Ala Lys Asp			
	835		840			845
Val His Arg Leu	Arg Gly Gln Ser Cys	Lys Glu	Pro Pro Glu Val Gln			
	850		855			860
Ser Phe Arg Glu	Lys Met Ala Phe	Phe Thr Arg	Pro Arg Met Asn Ile			
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Pro Ala Leu Ser	Ala Asp Asp Val					
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&lt;210&gt; 162

&lt;211&gt; 5794

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 162

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Lys Glu Arg Lys Ser Gln Gly Ala Gly Ser Gly Gln Asp Glu Ala Asp  
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&lt;210&gt; 165

&lt;211&gt; 421

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 165

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&lt;400&gt; 166

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 tgtctgcact gttcaaacct ctgccgccct ccacacctct aaacatctcc cctctcacct 1080  
 cattccccca cctatcccca ttctctgcct gtactgaagc tgaaatgcag gaagtgggtg 1140  
 caaaggttta ttccagagaa gccaggaagc cggtcatac ccagcctctg agagcagtta 1200  
 ctggggtcac ccaacctgac ttctctgcc actcccgcgt gtgtgacttt gggcaagcca 1260  
 agtgccctct ctgaacctca gtttctcat ctgcaaatg ggaacaatga cgtgcctacc 1320

180

tcttagacat gttgtgagga gactatgata taacatgtgt atgtaaatct tcatgtgatt 1380  
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 aaaaaaaaaa aaaa 1454

<210> 167  
 <211> 276  
 <212> PRT  
 <213> Homo sapiens

<400> 167  
 Met Arg Ala Pro His Leu His Leu Ser Ala Ala Ser Gly Ala Arg Ala  
 1 5 10 15  
 Leu Ala Lys Leu Leu Pro Leu Leu Met Ala Gln Leu Trp Ala Ala Glu  
 20 25 30  
 Ala Ala Leu Leu Pro Gln Asn Asp Thr Arg Leu Asp Pro Glu Ala Tyr  
 35 40 45  
 Gly Ala Pro Cys Ala Arg Gly Ser Gln Pro Trp Gln Val Ser Leu Phe  
 50 55 60  
 Asn Gly Leu Ser Phe His Cys Ala Gly Val Leu Val Asp Gln Ser Trp  
 65 70 75 80  
 Val Leu Thr Ala Ala His Cys Gly Asn Lys Pro Leu Trp Ala Arg Val  
 85 90 95  
 Gly Asp Asp His Leu Leu Leu Leu Gln Gly Glu Gln Leu Arg Arg Thr  
 100 105 110  
 Thr Arg Ser Val Val His Pro Lys Tyr His Gln Gly Ser Gly Pro Ile  
 115 120 125  
 Leu Pro Arg Arg Thr Asp Glu His Asp Leu Met Leu Leu Lys Leu Ala  
 130 135 140  
 Arg Pro Val Val Pro Gly Pro Arg Val Arg Ala Leu Gln Leu Pro Tyr  
 145 150 155 160  
 Arg Cys Ala Gln Pro Gly Asp Gln Cys Gln Val Ala Gly Trp Gly Thr  
 165 170 175  
 Thr Ala Ala Arg Arg Val Lys Tyr Asn Lys Gly Leu Thr Cys Ser Ser  
 180 185 190  
 Ile Thr Ile Leu Ser Pro Lys Glu Cys Glu Val Phe Tyr Pro Gly Val  
 195 200 205  
 Val Thr Asn Asn Met Ile Cys Ala Gly Leu Asp Arg Gly Gln Asp Pro  
 210 215 220  
 Cys Gln Ser Asp Ser Gly Gly Pro Leu Val Cys Asp Glu Thr Leu Gln  
 225 230 235 240  
 Gly Ile Leu Ser Trp Gly Val Tyr Pro Cys Gly Ser Ala Gln His Pro  
 245 250 255  
 Ala Val Tyr Thr Gln Ile Cys Lys Tyr Met Ser Trp Ile Asn Lys Val  
 260 265 270  
 Ile Arg Ser Asn  
 275

<210> 168  
 <211> 1506  
 <212> DNA  
 <213> Homo sapiens

<400> 168  
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 agcccggggc agggcgggg gccagtgtg tgacacacgc ttagctgtc tccccggctg 120  
 gctggctgc tctctctgg ggaacacagag gtcggcaggc agcacacaga gggacctacg 180  
 ggcagctgtt ctttccccg actcaagaat ccccgagggc ccggaggcct gcagcaggag 240



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cggccatgaa gaagctgatg gtggtgctga gtctgattgc tgcagcctgg gcagaggagc 300
agaataagtt ggtgcatggc ggaccctgcg acaagacatc tcacccttac caagctgcc 360
tctacacctc gggccacttg ctctgtggtg gggtccttat ccatccactg tgggtcctca 420
cagctgcccc ctgcaaaaaa ccgaatcttc aggtcttcct ggggaagcat aaccttcggc 480
aaagggagag ttcccaggag cagagttctg ttgtccgggc tgtgatccac cctgactatg 540
atgccgccag ccatgaccag gacatcatgc tgttgccgct ggcacgcca gccaaactct 600
ctgaactcat ccagcccctt cccctggaga gggactgctc agccaacacc accagctgcc 660
acatcctggg ctggggcaag acagcagatg gtgatttccc tgacaccatc cagtgtgcat 720
acatccacct ggtgtcccgt gaggagtgtg agcatgccta ccctggccag atcaccaga 780
acatgttgtg tgctggggag gagaagtacg ggaaggattc ctgccagggt gattctgggg 840
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gatcaaagga gaagccagga gtctacacca acgtctgcag atacacgaac tggatccaaa 960
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aagatgaaga taaggatgat acagtctcca tcaggcagtg gctgttgaa agatttaaga 1440
tttcacacct atgacataca tgggatagca cctgggcccgc catgcactca ataaagaatg 1500
tattttt 1506

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&lt;210&gt; 169

&lt;211&gt; 244

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 169

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Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Ala Trp Ala
 1          5          10          15
Glu Glu Gln Asn Lys Leu Val His Gly Gly Pro Cys Asp Lys Thr Ser
 20          25          30
His Pro Tyr Gln Ala Ala Leu Tyr Thr Ser Gly His Leu Leu Cys Gly
 35          40          45
Gly Val Leu Ile His Pro Leu Trp Val Leu Thr Ala Ala His Cys Lys
 50          55          60
Lys Pro Asn Leu Gln Val Phe Leu Gly Lys His Asn Leu Arg Gln Arg
 65          70          75          80
Glu Ser Ser Gln Glu Gln Ser Ser Val Val Arg Ala Val Ile His Pro
 85          90          95
Asp Tyr Asp Ala Ala Ser His Asp Gln Asp Ile Met Leu Leu Arg Leu
100          105          110
Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln Pro Leu Pro Leu Glu
115          120          125
Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His Ile Leu Gly Trp Gly
130          135          140
Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile Gln Cys Ala Tyr Ile
145          150          155          160
His Leu Val Ser Arg Glu Glu Cys Glu His Ala Tyr Pro Gly Gln Ile
165          170          175
Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys Tyr Gly Lys Asp Ser
180          185          190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Asp His Leu Arg
195          200          205
Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly Ser Lys Glu Lys Pro
210          215          220
Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn Trp Ile Gln Lys Thr

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225  
Ile Gln Ala Lys

230

235

240

<210> 170  
<211> 1641  
<212> DNA  
<213> Homo sapiens

<400> 170  
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caggtgcgcc tgagctccgc tcgccccggc ggccttggca gcagcagcct ctacggcctc 180  
ggcgccctcg ggccgcgcgt ggccgtgcgc tctgcctatg ggggcccggg gggcgccggc 240  
atccgcgagg tcaccattaa ccagagcctg ctggccccgc tgcggctgga cgccgacccc 300  
tccctccagc ggggtgcgca ggaggagagc gagcagatca agaccctcaa caacaagttt 360  
gcctccttca tcgacaaggt gcggtttctg gagcagcaga acaagctgct ggagaccaag 420  
tggagcgtcg tcgaggagca gaagtcggcc aagagcagcc gcctcccaga catctttgag 480  
gccagattg ctggccttcg gggtcagctt gaggcactgc aggtggatgg gggcgccctg 540  
gaggcgagc tgcggagcat gcaggatgtg gtggaggact tcaagaataa gtacgaagat 600  
gaaattaacc gccgcacagc tgctgagaat gaggttgtgg tgctgaagaa ggatgtggat 660  
gctgcctaca cgagcaaggt ggagctggag gccaaagtgg atgccctgaa tgatgagatc 720  
aacttcctca ggaccctcaa tgagacggag ttgacagagc tgcagtccca gatctccgac 780  
acatctgtgg tgctgtccat ggacaacagt cgctccctgg acctggacgg catcatcgct 840  
gagggtcaagg cacagtatga ggagatggcc aaatgcagcc gggctgaggc tgaagcctgg 900  
taccagacca agtttgagac cctccaggcc caggctggga agcatgggga cgacctccgg 960  
aatacccgga atgagatttc agagatgaac cgggcatcc agaggctgca ggctgagatc 1020  
gacaacatca agaaccagcg tgccaagtgg gaggcgcgca ttgccgaggc tgaggagcgt 1080  
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cgggccaagc aggatatggc acggcagctg cgtgagtacc aggaactcat gagcgtgaag 1200  
ctggccctgg acatcgagat cgccacctac cgcaagctgc tggaggcgca ggagagccgg 1260  
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agtcgcagga gtgcccgcga ctgagccgcc tcccaccact ccactcctcc agccaccacc 1500  
cacaatcaca agaagattcc caccctgcct tcccatgcct ggtcccaaga cagtgaaca 1560  
gtctggaag tgatgtcaga atagcttcca ataaagcagc ctcattctga ggcctgagt 1620  
atccaaaaaa aaaaaaaaaa a 1641

<210> 171  
<211> 469  
<212> PRT  
<213> Homo sapiens

<400> 171  
Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala  
1 5 10 15  
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly  
20 25 30  
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg  
35 40 45  
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg  
50 55 60  
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala  
65 70 75 80  
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys  
85 90 95

183

Ala Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu  
 100 105 110  
 Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu  
 115 120 125  
 Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln  
 130 135 140  
 Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly  
 145 150 155 160  
 Arg Leu Glu Gln Gly Leu Arg Thr Met Gln Asp Val Val Glu Asp Phe  
 165 170 175  
 Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn  
 180 185 190  
 Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys  
 195 200 205  
 Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe  
 210 215 220  
 Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile  
 225 230 235 240  
 Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp  
 245 250 255  
 Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala  
 260 265 270  
 Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu  
 275 280 285  
 Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr  
 290 295 300  
 Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala  
 305 310 315 320  
 Glu Ile Asp Asn Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile  
 325 330 335  
 Ala Glu Ala Glu Glu Cys Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala  
 340 345 350  
 Lys Gln Glu Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met  
 355 360 365  
 Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala  
 370 375 380  
 Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Glu Gly Glu Glu  
 385 390 395 400  
 Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met  
 405 410 415  
 Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu  
 420 425 430  
 Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly  
 435 440 445  
 Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg  
 450 455 460  
 Arg Ser Ala Arg Asp  
 465

&lt;210&gt; 172

&lt;211&gt; 1640

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 172

ggcagtgccg gctcctcctc gcccgccgct aggtccatcc cggcccagcc accatgtcca 60  
 tccacttcag ctccccggta ttcacctcgc gctcagccgc cttctcgggc cgcggcgccc 120

184

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aggtgcgct gagtccgct cgccccggcg gccttggcag cagcagcctc tacggcctcg 180
gcgcctcgcg gccgcgcgtg gccgtgcgct ctgcctatgg gggcccgggtg ggcgccggca 240
tccgcgaggt caccattaac cagagcctgc tggccccgct gcggctggac gccgaccct 300
ccctccagcg ggtgcgccag gaggagagcg agcagatcaa gacctcaac aacaagtttg 360
cctccttcat cgacaaggtg cggtttctgg agcagcagaa caagctgctg gagaccaagt 420
ggacgctgct gcaggagcag aagtcggcca agagcagccg cctcccagac atctttgagg 480
cccagattgc tggccttcgg ggtcagcttg aggcaactgca ggtggatggg ggccgcctgg 540
aggcggagct gcggagcatg caggatgtgg tggaggactt caagaataag tacgaagatg 600
aaattaaccg ccgcacagct gctgagaatg agtttgtggt gctgaagaag gatgtggatg 660
ctgcctacat gagcaaggtg gagctggagg ccaaggtgga tgcctgaat gatgagatca 720
acttcctcag gacctcaat gagacggagt tgacagagct gcagtcaccag atctccgaca 780
catctgtggt gctgtccatg gacaacagtc gctccctgga cctggacggc atcatcgctg 840
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acaatcacia gaagattccc acccctgcct cccatgcctg gtccaagac agtgagacag 1560
tctggaaagt gatgtcagaa tagcttccaa taaagcagcc tcattctgag gcctgagtga 1620
tccaaaaaaa aaaaaaaaaa 1640

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&lt;210&gt; 173

&lt;211&gt; 469

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 173

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Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala
1           5           10           15
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly
20           25           30
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg
35           40           45
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg
50           55           60
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala
65           70           75           80
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Ser Glu Gln Ile Lys
85           90           95
Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
100          105          110
Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu
115          120          125
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln
130          135          140
Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly
145          150          155          160
Arg Leu Glu Ala Glu Leu Arg Ser Met Gln Asp Val Val Glu Asp Phe
165          170          175
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn
180          185          190
Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys

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195	200	205
Val Glu Leu Glu Ala Lys	Val Asp Ala Leu Asn	Asp Glu Ile Asn Phe
210	215	220
Leu Arg Thr Leu Asn Glu Thr	Glu Leu Thr Glu Leu Gln Ser Gln Ile	
225	230	235
Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp		240
245	250	255
Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala		260
260	265	270
Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu		275
275	280	285
Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr		290
290	295	300
Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala		305
305	310	315
Glu Ile Asp Asn Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile		320
325	330	335
Ala Glu Ala Glu Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala		340
340	345	350
Lys Gln Glu Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met		355
355	360	365
Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala		370
370	375	380
Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu		385
385	390	395
Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met		400
405	410	415
Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu		420
420	425	430
Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ala Gly		435
435	440	445
Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg		450
450	455	460
Arg Ser Ala Arg Asp		
465		

&lt;210&gt; 174

&lt;211&gt; 2186

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 174

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aacgggacca aggagtctaa cacgtgcgcg agtcgggggc tcgcacgaaa gccgccgtgg 60
cgcaatgaag gtgaaggccg gcgcgctcgc cgcccgaggt gggatcccga ggccctctcca 120
gtccgcccag ggcgaccac cggcccgtct cgcccgcgc gccggggagg tggagcacga 180
gcgcacgtgt taggaccga aagatggtga actatgcctg gccagggcga agccagagga 240
aactctggtg gaggtccgta gcggtcctga cgtgcaaata ggtcgtccga cctgggtata 300
ggggcgggct ccaggcgagg cggtcgacgc tcctgaaaac ttgcgcgcgc gctcgcgcca 360
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gcttgtgctg ccatgtccgc accggcacca tcctgctcgg cgtctggtat ctgatcatca 480
atgctgtggt actgttgatt ttattgagtg ccctggctga tccggatcag tataactttt 540
caagttctga actgggaggt gactttgagt tcatggatga tgccaacatg tgcattgcca 600
ttgcgatttc tcttctcatg atcctgatat gtgctatggc tacttacgga gcgtacaagc 660
aacgcgcagc ctggatcatc ccattcttct gttaccagat ctttgacttt gccctgaaca 720
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tgctcctaa ttttcctac agagatgatg tcatgtcagt gaatcctacc tgtttggtcc 840
ttattattct tctgtttatt agcattatct tgacttttaa gggttacttg attagctgtg 900

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cagcagcttg actttgcaga catctgagca atagttctgt tatttcaactt ttgcatagag 1140
cctctctgag cttgtttgtt gctgaaatgc tactttttta aatttagatg ttagattgaa 1200
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ggaaaagggt tttcttttcc ctgcaagcta catcctactg ctttgaactt ccaagtatgt 1980
ctagtcacct tttaaaatgt aaacattttc agaaaaatga ggattgcctt ccttgtatgc 2040
gctttttacc tctgactacct gaattgcaag ggatttttat atattcatat gttacaaagt 2100
cagcaactct cctgttggtt cattattgaa tgtgctgtaa attaatgtgt ttgcaattaa 2160
aacaaggttt gcccaaaaa aaaaaa 2186

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&lt;210&gt; 175

&lt;211&gt; 283

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 175

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Met Val Asn Tyr Ala Trp Ala Gly Arg Ser Gln Arg Lys Leu Trp Trp
 1          5          10          15
Arg Ser Val Ala Val Leu Thr Cys Lys Ser Val Val Arg Pro Gly Tyr
 20          25          30
Arg Gly Gly Leu Gln Ala Arg Arg Ser Thr Leu Leu Lys Thr Cys Ala
 35          40          45
Arg Ala Arg Ala Thr Ala Pro Gly Ala Met Lys Met Val Ala Pro Trp
 50          55          60
Thr Arg Phe Tyr Ser Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr
 65          70          75          80
Gly Thr Ile Leu Leu Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val
 85          90          95
Leu Leu Ile Leu Leu Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe
100          105          110
Ser Ser Ser Glu Leu Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn
115          120          125
Met Cys Ile Ala Ile Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala
130          135          140
Met Ala Thr Tyr Gly Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro
145          150          155          160
Phe Phe Cys Tyr Gln Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala
165          170          175
Ile Thr Val Leu Ile Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln
180          185          190
Leu Pro Pro Asn Phe Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro
195          200          205
Thr Cys Leu Val Leu Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr
210          215          220
Phe Lys Gly Tyr Leu Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile

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<210> 176
<211> 597
<212> DNA
<213> Homo sapiens
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<400> 176						
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caggactcca	cctcagacct	gatcccagcc	ccacctctga	gcaagggtccc	tctgcagcag	120
aacttccagg	acaaccaatt	ccaggggaag	tggtatgtgg	taggcctggc	agggaatgca	180
attctcagag	aagacaaaga	cccgcaaaag	atgtatgcc	ccatctatga	gctgaaagaa	240
gacaagagct	acaatgtcac	ctccgtcctg	tttaggaaaa	agaagtgtga	ctactggatc	300
aggacttttg	ttccagggtt	ccagcccggc	gagttcacgc	tgggcaacat	taagagttac	360
cctggattaa	cgagttacct	cgtccagagt	gtgagcacca	actacaacca	gcatgctatg	420
gtgttcttca	agaaagtttc	tcaaaacagg	gagtaacttca	agatcacccct	ctacggggaga	480
accaaggagc	tgactttcgg	actaaaggag	aactcatcc	gcttctccaa	atatctgggc	540
ctccctgaaa	accacatcgt	cttcctctgc	ccaatcgacc	agtgtatcga	cggctga	597

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<210> 177
<211> 198
<212> PRT
<213> Homo sapiens
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<400>	177
Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu	
1                      5                      10                      15	
His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro	
20                      25                      30	
Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln	
35                      40                      45	
Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu	
50                      55                      60	
Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu	
65                      70                      75                      80	
Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys	
85                      90                      95	
Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe	
100                      105                      110	
Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val	
115                      120                      125	
Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys	
130                      135                      140	
Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg	
145                      150                      155                      160	
Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser	
165                      170                      175	
Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile	
180                      185                      190	
Asp Gln Cys Ile Asp Gly	
195	

<210> 178  
 <211> 1518  
 <212> DNA  
 <213> Homo sapiens

<400> 178  
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 gggcagcacc atgcagcccc tgtggetctg ctgggcactc tgggtgttgc ccctggccag 120  
 ccccggggcc gccctgaccg gggagcagct cctgggcagc ctgctgcggc agctgcagct 180  
 caaagagggtg cccaccctgg acagggccga catggaggag ctggatcatc ccaccacgt 240  
 gagggcccag tacgtggccc tgctgcagcg cagccacggg gaccgctccc gcggaaagag 300  
 gttcagccag agcttccgag aggtggccgg caggttctct gcgttgaggg ccagcacaca 360  
 cctgctggtg ttccgcatgg agcagcggct gccgcccaac agcagctggg tcagggccgt 420  
 gctgcggctc ttccaggagc cggccccaa ggccgcgctg cacaggcacg ggcggctgtc 480  
 cccgcgcagc gcccgggccc gggtgaccgt cgagtggctg cgcgtccgcg acgacggctc 540  
 caaccgcacc tccctcatcg actccaggct ggtgtccgtc cacgagagcg gctggaaggc 600  
 cttcgacgtg accgaggccg tgaacttctg gcagcagctg agccggcccc ggcagccgt 660  
 gctgctacag gtgtcgggtg agagggagca tctgggcccg ctggcgtccg gcgccacaa 720  
 gctgggtccgc tttgcctcgc agggggcgcc agccgggctt ggggagcccc agctggagct 780  
 gcacaccctg gaccttgggg actatggagc tcaggggcag tgtgaccctg aagcaccaat 840  
 gaccgagggc acccgctgct gccgccagga gatgtacatt gacctgcagg ggatgaagt 900  
 ggccgagaac tgggtgctgg agccccggg cttcctggct tatgagtgtg tgggcacctg 960  
 ccggcagccc ccggaggccc tggccttcaa gtggccgttt ctggggcctc gacagtgc 1020  
 cgctcggag actgactcgc tgcccattgat cgtcagcatc aaggaggagg gcaggaccag 1080  
 gccccagggtg gtcagcctgc ccaacatgag ggtgcagaag tgcagctgtg cctcggatgg 1140  
 tgcgctcgtg ccaaggaggc tccagccata ggcgcctagt gtagccatcg agggacttga 1200  
 cttgtgtgtg tttctgaagt gttcgagggt accaggagag ctggcgatga ctgaactgct 1260  
 gatggacaaa tgctctgtgc tctctagtga gccctgaatt tgcttctct gacaagtta 1320  
 ctcacctaatt tttgtcttct caggaatgag aatctttggc cactggagag cccttgctca 1380  
 gttttctcta ttcttattat tcaactgact atattctaag cacttacatg tggagatact 1440  
 gtaacctgag ggcagaaagc ccaatgtgtc attgtttact tgtcctgtca ctggatctgg 1500  
 gctaaagtcc tccaccac 1518

<210> 179  
 <211> 366  
 <212> PRT  
 <213> Homo sapiens

<400> 179  
 Met Gln Pro Leu Trp Leu Cys Trp Ala Leu Trp Val Leu Pro Leu Ala  
 1 5 10 15  
 Ser Pro Gly Ala Ala Leu Thr Gly Glu Gln Leu Leu Gly Ser Leu Leu  
 20 25 30  
 Arg Gln Leu Gln Leu Lys Glu Val Pro Thr Leu Asp Arg Ala Asp Met  
 35 40 45  
 Glu Glu Leu Val Ile Pro Thr His Val Arg Ala Gln Tyr Val Ala Leu  
 50 55 60  
 Leu Gln Arg Ser His Gly Asp Arg Ser Arg Gly Lys Arg Phe Ser Gln  
 65 70 75 80  
 Ser Phe Arg Glu Val Ala Gly Arg Phe Leu Ala Leu Glu Ala Ser Thr  
 85 90 95  
 His Leu Leu Val Phe Gly Met Glu Gln Arg Leu Pro Pro Asn Ser Glu  
 100 105 110  
 Leu Val Gln Ala Val Leu Arg Leu Phe Gln Glu Pro Val Pro Lys Ala  
 115 120 125  
 Ala Leu His Arg His Gly Arg Leu Ser Pro Arg Ser Ala Arg Ala Arg



189

130		135		140
Val Thr Val Glu Trp	Leu Arg Val Arg Asp Asp	Gly Ser Asn Arg Thr		
145	150	155	160	
Ser Leu Ile Asp	Ser Arg Leu Val Ser Val His	Glu Ser Gly Trp Lys		
	165	170	175	
Ala Phe Asp Val Thr	Glu Ala Val Asn Phe Trp	Gln Gln Leu Ser Arg		
	180	185	190	
Pro Arg Gln Pro	Leu Leu Leu Gln Val Ser Val	Gln Arg Glu His Leu		
	195	200	205	
Gly Pro Leu Ala	Ser Gly Ala His Lys Leu Val	Arg Phe Ala Ser Gln		
	210	215	220	
Gly Ala Pro Ala	Gly Leu Gly Glu Pro Gln Leu	Glu Leu His Thr Leu		
225	230	235	240	
Asp Leu Gly Asp	Tyr Gly Ala Gln Gly Asp Cys	Asp Pro Glu Ala Pro		
	245	250	255	
Met Thr Glu Gly	Thr Arg Cys Cys Arg Gln Glu	Met Tyr Ile Asp Leu		
	260	265	270	
Gln Gly Met Lys	Trp Ala Glu Asn Trp Val Leu	Glu Pro Pro Gly Phe		
	275	280	285	
Leu Ala Tyr Glu	Cys Val Gly Thr Cys Arg Gln	Pro Pro Glu Ala Leu		
	290	295	300	
Ala Phe Lys Trp	Pro Phe Leu Gly Pro Arg Gln	Cys Ile Ala Ser Glu		
305	310	315	320	
Thr Asp Ser Leu	Pro Met Ile Val Ser Ile Lys	Glu Gly Gly Arg Thr		
	325	330	335	
Arg Pro Gln Val	Val Ser Leu Pro Asn Met Arg	Val Gln Lys Cys Ser		
	340	345	350	
Cys Ala Ser Asp	Gly Ala Leu Val Pro Arg Arg	Leu Gln Pro		
	355	360	365	

&lt;210&gt; 180

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 180

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aattctagaa gtccaaatca ctcattgttt gtgaaagctg agctcacagc aaaacaagcc 60
accatgaagc tgctcggtgtg tctcctgctg gtcacgctgg ccctctgctg ctaccaggcc 120
aatgccgagt tctgcccagc tcttgtttct gagctgttag acttcttctt cattagttaa 180
cctctgttca agttaagtct tgccaaattt gatgccctc cggaagctgt tgcagccaag 240
ttaggagtga agagatgcac ggatcagatg tcccttcaga aacgaagcct cattgcggaa 300
gtcctggtga aaatattgaa gaaatgtagt gtgtgacatg taaaaacttt catcctggtt 360
tccactgtct ttcaatgaca ccctgatctt cactgcagaa tgtaaagggt tcaacgtctt 420
gctttaataa atcacttgct ctac                                     444

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&lt;210&gt; 181

&lt;211&gt; 90

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 181

Met Lys Leu Ser Val	Cys Leu Leu Leu Val Thr	Leu Ala Leu Cys Cys
1	5	10
Tyr Gln Ala Asn Ala	Glu Phe Cys Pro Ala Leu Val	Ser Glu Leu Leu
	20	25
Asp Phe Phe Phe Ile	Ser Glu Pro Leu Phe Lys	Leu Ser Leu Ala Lys
	35	40
		45

190

Phe Asp Ala Pro Pro Glu Ala Val Ala Ala Lys Leu Gly Val Lys Arg  
 50 55 60  
 Cys Thr Asp Gln Met Ser Leu Gln Lys Arg Ser Leu Ile Ala Glu Val  
 65 70 75 80  
 Leu Val Lys Ile Leu Lys Lys Cys Ser Val  
 85 90

<210> 182  
 <211> 754  
 <212> DNA  
 <213> Homo sapiens

<400> 182  
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 gtccaagctg caagatgacc tcaaggaggc aatgaatact atgatgtgta gccgatgccca 120  
 aggaaagcat aggaggtttg aaatggaccg ggaacctaa agtgccagat actgtgctga 180  
 gtgtaatagg ctgcatcctg ctgaggaagg agacttttgg gcagagtcaa gcatgttggg 240  
 cctcaagatc acctactttg cactgatgga tggaaagggtg tatgacatca cagagtgggc 300  
 tggatgccag cgtgtaggta tctccccaga taccacaga gtcccctatc acatctcatt 360  
 tggttctcgg attccaggca ccagaggcg gcagagagcc accccagatg cccctcctgc 420  
 tgatcttcag gatttcttga gtcggatctt tcaagtaccc ccagggcaga tgccaatggg 480  
 aacttctttg cagctcctca gcctgccctt ggagccgctg cagcctctaa gcccaacagc 540  
 acagtaccca agggagaagc caaacctaag cggcggaaga aagtgaggag gcccttccaa 600  
 cgttgatgcc ctttctcttt cttcaaatca atgtcagggg gtcaaaaggg ctgtagcaca 660  
 ggatggagtt tgatttatcc ctctccccc aacacctagg aactgaatct ttttcttttt 720  
 attttttgag atggagtctt gctctgttgc ccag 754

<210> 183  
 <211> 191  
 <212> PRT  
 <213> Homo sapiens

<400> 183  
 Met Lys Arg Met Ala Glu Asn Glu Leu Ser Arg Ser Val Asn Glu Phe  
 1 5 10 15  
 Leu Ser Lys Leu Gln Asp Asp Leu Lys Glu Ala Met Asn Thr Met Met  
 20 25 30  
 Cys Ser Arg Cys Gln Gly Lys His Arg Arg Phe Glu Met Asp Arg Glu  
 35 40 45  
 Pro Lys Ser Ala Arg Tyr Cys Ala Glu Cys Asn Arg Leu His Pro Ala  
 50 55 60  
 Glu Glu Gly Asp Phe Trp Ala Glu Ser Ser Met Leu Gly Leu Lys Ile  
 65 70 75 80  
 Thr Tyr Phe Ala Leu Met Asp Gly Lys Val Tyr Asp Ile Thr Glu Trp  
 85 90 95  
 Ala Gly Cys Gln Arg Val Gly Ile Ser Pro Asp Thr His Arg Val Pro  
 100 105 110  
 Tyr His Ile Ser Phe Gly Ser Arg Ile Pro Gly Thr Arg Gly Arg Gln  
 115 120 125  
 Arg Ala Thr Pro Asp Ala Pro Pro Ala Asp Leu Gln Asp Phe Leu Ser  
 130 135 140  
 Arg Ile Phe Gln Val Pro Pro Gly Gln Met Pro Met Gly Thr Ser Leu  
 145 150 155 160  
 Gln Leu Leu Ser Leu Pro Leu Glu Pro Leu Gln Pro Leu Ser Pro Thr  
 165 170 175  
 Ala Gln Tyr Pro Arg Glu Lys Pro Asn Leu Ser Gly Gly Arg Lys  
 180 185 190

<210> 184  
 <211> 2511  
 <212> DNA  
 <213> Homo sapiens

<400> 184  
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 ggccgatggc gcaaaggtag gacgatctac cccattacgg gggcatggat ggagtaggca 120  
 tcccctccac gatgtatggg gaccgcgatg cagccagggtc catgcagccg gtccaccacc 180  
 tgaaccacgg gcctcctctg cactcgcatac agtaccgcga cacagctcat accaaccgca 240  
 tggcccccag catgggctcc tctgtcaatg acgctttaaa gagagataaa gatgccattt 300  
 atggacaccc cctcttccct ctcttagcac tgatttttga gaaatgtgaa ttagctactt 360  
 gtaccccccg cgagccgggg gtggcggggc gggacgtctg ctcgtcagag tcattcaatg 420  
 aagatatagc cgtgttcgcc aaacagattc gcgcagaaaa acctctattt tcttctaatac 480  
 cagaactgga taacttgatg attcaagcca tacaagtatt aagggttcat ctattggaat 540  
 tagagaaggt acacgaatta tgtgacaatt tctgccaccg gtatatttagc tgtttgaaag 600  
 ggaaaatgcc tatcgatttg gtgatagacg atagagaagg aggatcaaaa tcagacagtg 660  
 aagatataac aagatcagca aatctaactg accagccctc ttggaacaga gatcatgatg 720  
 acacggcatc tactcgttca ggaggaaccc caggcccttc cagcgggtggc cacacgtcac 780  
 acagtgggga caacagcagt gagcaaggtg atggccttga caacagtgtg gcttcccca 840  
 gcacaggtga cgatgatgac cctgataagg acaaaaagcg tcacaaaaag cgtggcatct 900  
 ttcccaaagt agccacaaat atcatgaggg cgtggctgtt ccagcatcta acacaccctt 960  
 acccttctga agaacagaaa aagcagttgg cacaagacac gggactcacc atccttcaag 1020  
 tgaacaattg gtttattaat gcccgagaa gaatagtgc gccatgata gaccagtcca 1080  
 accgagcagt aagtcaagga acacettata atcctgatgg acagcccatg ggaggtttcg 1140  
 taatggacgg tcagcaacat atgggaatta gagcaccagg acctatgagt ggaatgggca 1200  
 tgaatatggg catggagggg cagtggcact acatgtaacc ttcactagt taaccaactg 1260  
 caaagcaagg gggaaggctg caaagtatgc caggggagta tgtagcccg ggtgggtcaa 1320  
 tgggtgtgag tatgggacag ccaagttata cccaacocca gatgcccccc catcctgctc 1380  
 agctgcgtca tgggcccccc atgcatacgt acattcctgg acaccctcac caccacaacag 1440  
 tgatgatgca tggaggaccg cccaccctg gaatgccaat gtcagcatca agccccacag 1500  
 ttcttaatac aggagaccga acaatgagtg gacaagtcac ggacattcat gctcagtagc 1560  
 ttaagggaaat atgcattgtc tgcaatgggt actgatttca aatcatgttt tttctgcaat 1620  
 gactgtggag ttccattctt ggcatctact ctggaccaag gagcatccct aattcttcat 1680  
 agggaccttt aaaaagcagg aaataccaac tgaagtcaat ttgggggaca tgctaaataa 1740  
 ctatataaga cattaaagga acaaagagtg aaatattgta aatgctatta tactgttatc 1800  
 catattacgt tgtttcttat agatttttta aaaaaaatgt gaaatttttc cactatgt 1860  
 gtgttgtttc catagctctt cacttctctc agaagcctcc ttacattaaa aagccttaca 1920  
 gttatcctgc aaggacaggg aaggtctgat ttgcaggatt tttagagcat taaaataact 1980  
 atcaggcaga agaactcttc ttctcgccta ggatttcagc catgcgcgcg ctctctctct 2040  
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 ttcatctact caccataatt gaattggcct gaacagatgt aaatcgggaa ggatgggaaa 2160  
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 tcattgtccc catgcaacaa ccaccacctt atacatcact tcctgtttta agcagctcta 2340  
 aaacatagac tgaagattta tttttaatat gttgacttta tttctgagca aagcatcggg 2400  
 catgtgtgta ttttttcata gtccacctt ggagcattta tgtagacatt gtaaataaat 2460  
 tttgtgcaaa aaggactgga aaaatgaact gtattattgc aatttttttt t 2511

<210> 185  
 <211> 390  
 <212> PRT  
 <213> Homo sapiens

<400> 185  
 Met Ala Gln Arg Tyr Asp Asp Leu Pro His Tyr Gly Gly Met Asp Gly

192

1	5	10	15
Val Gly Ile Pro Ser Thr Met Tyr Gly Asp Pro His Ala Ala Arg Ser			
20		25	30
Met Gln Pro Val His His Leu Asn His Gly Pro Pro Leu His Ser His			
35		40	45
Gln Tyr Pro His Thr Ala His Thr Asn Ala Met Ala Pro Ser Met Gly			
50		55	60
Ser Ser Val Asn Asp Ala Leu Lys Arg Asp Lys Asp Ala Ile Tyr Gly			
65	70	75	80
His Pro Leu Phe Pro Leu Leu Ala Leu Ile Phe Glu Lys Cys Glu Leu			
85		90	95
Ala Thr Cys Thr Pro Arg Glu Pro Gly Val Ala Gly Gly Asp Val Cys			
100		105	110
Ser Ser Glu Ser Phe Asn Glu Asp Ile Ala Val Phe Ala Lys Gln Ile			
115		120	125
Arg Ala Glu Lys Pro Leu Phe Ser Ser Asn Pro Glu Leu Asp Asn Leu			
130		135	140
Met Ile Gln Ala Ile Gln Val Leu Arg Phe His Leu Leu Glu Leu Glu			
145	150	155	160
Lys Val His Glu Leu Cys Asp Asn Phe Cys His Arg Tyr Ile Ser Cys			
165		170	175
Leu Lys Gly Lys Met Pro Ile Asp Leu Val Ile Asp Asp Arg Glu Gly			
180		185	190
Gly Ser Lys Ser Asp Ser Glu Asp Ile Thr Arg Ser Ala Asn Leu Thr			
195		200	205
Asp Gln Pro Ser Trp Asn Arg Asp His Asp Asp Thr Ala Ser Thr Arg			
210		215	220
Ser Gly Gly Thr Pro Gly Pro Ser Ser Gly Gly His Thr Ser His Ser			
225	230	235	240
Gly Asp Asn Ser Ser Glu Gln Gly Asp Gly Leu Asp Asn Ser Val Ala			
245		250	255
Ser Pro Ser Thr Gly Asp Asp Asp Asp Pro Asp Lys Asp Lys Lys Arg			
260		265	270
His Lys Lys Arg Gly Ile Phe Pro Lys Val Ala Thr Asn Ile Met Arg			
275		280	285
Ala Trp Leu Phe Gln His Leu Thr His Pro Tyr Pro Ser Glu Glu Gln			
290		295	300
Lys Lys Gln Leu Ala Gln Asp Thr Gly Leu Thr Ile Leu Gln Val Asn			
305	310	315	320
Asn Trp Phe Ile Asn Ala Arg Arg Arg Ile Val Gln Pro Met Ile Asp			
325		330	335
Gln Ser Asn Arg Ala Val Ser Gln Gly Thr Pro Tyr Asn Pro Asp Gly			
340		345	350
Gln Pro Met Gly Gly Phe Val Met Asp Gly Gln Gln His Met Gly Ile			
355		360	365
Arg Ala Pro Gly Pro Met Ser Gly Met Gly Met Asn Met Gly Met Glu			
370		375	380
Gly Gln Trp His Tyr Met			
385	390		

&lt;210&gt; 186

&lt;211&gt; 517

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 186

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193

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cgccatgaag ctgctgatgg tctcatgctt ggcggccctc ctctgcact gctatgcaga 120
ttctggctgc aaactcctgg aggacatggt tgaaaagacc atcaattccg acatatctat 180
acctgaatac aaagagcttc ttcaagagtt catagacagt gatgccgctg cagaggctat 240
ggggaaattc aagcagtgtt tctcaacca gtcacataga actctgaaa actttggact 300
gatgatgcat acagtgtacg acagcatttg gtgtaatatg aagagtaatt aactttaccc 360
aaggcgtttg gctcagaggg ctacagacta tggccagaac tcactgtgtg attgctagaa 420
accacttttc tttcttgtgt tgtcttttta tgtggaaact gctagacaac tgttgaaacc 480
tcaaattcat ttccatttca ataactaact gcaaatc 517

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&lt;210&gt; 187

&lt;211&gt; 95

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 187

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Met Lys Leu Leu Met Val Leu Met Leu Ala Ala Leu Leu Leu His Cys
 1             5             10             15
Tyr Ala Asp Ser Gly Cys Lys Leu Leu Glu Asp Met Val Glu Lys Thr
      20             25             30
Ile Asn Ser Asp Ile Ser Ile Pro Glu Tyr Lys Glu Leu Leu Gln Glu
      35             40             45
Phe Ile Asp Ser Asp Ala Ala Ala Glu Ala Met Gly Lys Phe Lys Gln
      50             55             60
Cys Phe Leu Asn Gln Ser His Arg Thr Leu Lys Asn Phe Gly Leu Met
      65             70             75             80
Met His Thr Val Tyr Asp Ser Ile Trp Cys Asn Met Lys Ser Asn
      85             90             95

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&lt;210&gt; 188

&lt;211&gt; 2048

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 188

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ctctgcaaac gccgcgttcc cggggtcccg cggctcccg cgcgcgctctg ccgcgcccg 60
ctgctgggca aaaatcagag ccgcctccgc cccattacc atcatggaaa ccctccagga 120
aaaagtggcc ccggacgcgc gagcctgagg attctgcaca aaagagggtg ccaaaatgaa 180
gacctgatg cgccatggtc tggcagtgtg tttagcgctc accaccatgt gcaccagctt 240
gttgctagtg tacagcagcc tcggcggcca gaaggagcgg ccccgccagc agcagcagca 300
gcagcagcaa cagcagcagc aggcgtcggc caccggcagc tcgcagccgg cggcggagag 360
cagcaccagc cagcgcgccg ggggtcccg cggaccggc cactggagc gatacctcg 420
agtggcggac cacaagcccc tgaaaatgca ctgcagggac tgtgccctgg tgaccagctc 480
aggcatctg ctgcacagtc ggcaaggctc ccagattgac cagacagagt gtgtcatccg 540
catgaatgac gccccacac gcggtatg gctgacgtg ggcaatcgca ccagcctgag 600
ggtcatcgcg cattccagca tccagaggat cctccgcaac cgccatgacc tgctcaacgt 660
gagccagggc accgtgttca tcttctgggg ccccgagcgc tacatgcggc gggacggcaa 720
gggcccaggc tacaacaacc tgcattctct gagccagggt ctgccccggc tgaaggcctt 780
catgattact cgccacaaga tgctgcagtt tgatgagctc ttcaagcagg agactggcaa 840
agacaggaag atatccaaca cttggctcag cactggctgg tttacaatga caattgcact 900
ggagctctgt gacaggatca atgtttatgg catggtgccc ccagacttct gcagggatcc 960
caatcaccct tcagtacctt atcattatta tgaacctttt ggacctgatg aatgtacaat 1020
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agtctttaag aactgggcac ggacattcaa tattcacttt tttcaaccag actggaaacc 1140
agaatacctt cctataaatc atcctgagaa taaacctgtg ttctaaggaa tgagcatggc 1200
agactgtaat cccaggtatt cactgcatca gacacggaga cactgaactt cctgagccac 1260
cagacaggaa agggtagcag aaaacagctt cactcctcag gaagtaccat ggacagacgc 1320
ctaccagggg tgacaaagca gtgcagttgg attgtaagga aaaattccgg aattaatgca 1380

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tcctaataagaa tgttgtcccc ttcaatgggt ttaccttagg agctgaacat tcaattcagt 1440
tacaccacta tgactaaaaa cagtttggat ctcttagtat tgcctttgaa actgcaacat 1500
aagcaactca acaatattag ttgcattcct ttatagacat accatgtcaa agacgttttt 1560
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aaaaaaaaa 2048

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&lt;210&gt; 189

&lt;211&gt; 336

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 189

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Met Lys Thr Leu Met Arg His Gly Leu Ala Val Cys Leu Ala Leu Thr
 1           5           10           15
Thr Met Cys Thr Ser Leu Leu Leu Val Tyr Ser Ser Leu Gly Gly Gln
 20           25           30
Lys Glu Arg Pro Pro Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln
 35           40           45
Gln Ala Ser Ala Thr Gly Ser Ser Gln Pro Ala Ala Glu Ser Ser Thr
 50           55           60
Gln Gln Arg Pro Gly Val Pro Ala Gly Pro Arg Pro Leu Asp Gly Tyr
 65           70           75           80
Leu Gly Val Ala Asp His Lys Pro Leu Lys Met His Cys Arg Asp Cys
 85           90           95
Ala Leu Val Thr Ser Ser Gly His Leu Leu His Ser Arg Gln Gly Ser
 100          105          110
Gln Ile Asp Gln Thr Glu Cys Val Ile Arg Met Asn Asp Ala Pro Thr
 115          120          125
Arg Gly Tyr Gly Arg Asp Val Gly Asn Arg Thr Ser Leu Arg Val Ile
 130          135          140
Ala His Ser Ser Ile Gln Arg Ile Leu Arg Asn Arg His Asp Leu Leu
 145          150          155          160
Asn Val Ser Gln Gly Thr Val Phe Ile Phe Trp Gly Pro Ser Ser Tyr
 165          170          175
Met Arg Arg Asp Gly Lys Gly Gln Val Tyr Asn Asn Leu His Leu Leu
 180          185          190
Ser Gln Val Leu Pro Arg Leu Lys Ala Phe Met Ile Thr Arg His Lys
 195          200          205
Met Leu Gln Phe Asp Glu Leu Phe Lys Gln Glu Thr Gly Lys Asp Arg
 210          215          220
Lys Ile Ser Asn Thr Trp Leu Ser Thr Gly Trp Phe Thr Met Thr Ile
 225          230          235          240
Ala Leu Glu Leu Cys Asp Arg Ile Asn Val Tyr Gly Met Val Pro Pro
 245          250          255
Asp Phe Cys Arg Asp Pro Asn His Pro Ser Val Pro Tyr His Tyr Tyr
 260          265          270
Glu Pro Phe Gly Pro Asp Glu Cys Thr Met Tyr Leu Ser His Glu Arg
 275          280          285
Gly Arg Lys Gly Ser His His Arg Phe Ile Thr Glu Lys Arg Val Phe
 290          295          300
Lys Asn Trp Ala Arg Thr Phe Asn Ile His Phe Phe Gln Pro Asp Trp

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305                      310                      315                      320  
Lys Pro Glu Ser Leu Ala Ile Asn His Pro Glu Asn Lys Pro Val Phe  
                        325                      330                      335

<400> 190					
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gttgcagaat	actcactatt	tccaaatagc	ccaaaatgga	cttccaaagt	ggtcacctac 360
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<400> 191															
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Ala	Leu	Pro	Leu	Pro	Gln	Glu	Ala	Gly	Gly	Met	Ser	Glu	Leu	Gln	Trp
			20					25					30		
Glu	Gln	Ala	Gln	Asp	Tyr	Leu	Lys	Arg	Phe	Tyr	Leu	Tyr	Asp	Ser	Glu
		35					40					45			
Thr	Lys	Asn	Ala	Asn	Ser	Leu	Glu	Ala	Lys	Leu	Lys	Glu	Met	Gln	Lys
	50					55					60				
Phe	Phe	Gly	Leu	Pro	Ile	Thr	Gly	Met	Leu	Asn	Ser	Arg	Val	Ile	Glu
65					70					75				80	
Ile	Met	Gln	Lys	Pro	Arg	Cys	Gly	Val	Pro	Asp	Val	Ala	Glu	Tyr	Ser
				85					90					95	
Leu	Phe	Pro	Asn	Ser	Pro	Lys	Trp	Thr	Ser	Lys	Val	Val	Thr	Tyr	Arg
			100					105					110		
Ile	Val	Ser	Tyr	Thr	Arg	Asp	Leu	Pro	His	Ile	Thr	Val	Asp	Arg	Leu
		115					120					125			
Val	Ser	Lys	Ala	Leu	Asn	Met	Trp	Gly	Lys	Glu	Ile	Pro	Leu	His	Phe
		130				135					140				
Arg	Lys	Val	Val	Trp	Gly	Thr	Ala	Asp	Ile	Met	Ile	Gly	Phe	Ala	Arg
145					150					155				160	
Gly	Ala	His	Gly	Asp	Ser	Tyr	Pro	Phe	Asp	Gly	Pro	Gly	Asn	Thr	Leu
				165					170					175	

196

Ala His Ala Phe Ala Pro Gly Thr Gly Leu Gly Gly Asp Ala His Phe  
 180 185 190  
 Asp Glu Asp Glu Arg Trp Thr Asp Gly Ser Ser Leu Gly Ile Asn Phe  
 195 200 205  
 Leu Tyr Ala Ala Thr His Glu Leu Gly His Ser Leu Gly Met Gly His  
 210 215 220  
 Ser Ser Asp Pro Asn Ala Val Met Tyr Pro Thr Tyr Gly Asn Gly Asp  
 225 230 235 240  
 Pro Gln Asn Phe Lys Leu Ser Gln Asp Asp Ile Lys Gly Ile Gln Lys  
 245 250 255  
 Leu Tyr Gly Lys Arg Ser Asn Ser Arg Lys Lys  
 260 265

&lt;210&gt; 192

&lt;211&gt; 2217

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 192

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<210> 193  
 <211> 702  
 <212> PRT  
 <213> Homo sapiens

<400> 193

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Ala	Leu	Gly	Ser	Leu	Leu	Phe	Leu	Leu	Phe	Ser	Leu	Gly	Trp	Val	Gln
		20						25					30		
Pro	Ser	Arg	Thr	Leu	Ala	Gly	Glu	Thr	Gly	Gln	Glu	Ala	Ala	Pro	Leu
		35					40					45			
Asp	Gly	Val	Leu	Ala	Asn	Pro	Pro	Asn	Ile	Ser	Ser	Leu	Ser	Pro	Arg
	50					55					60				
Gln	Leu	Leu	Gly	Phe	Pro	Cys	Ala	Glu	Val	Ser	Gly	Leu	Ser	Thr	Glu
65					70					75				80	
Arg	Val	Arg	Glu	Leu	Ala	Val	Ala	Leu	Ala	Gln	Lys	Asn	Val	Lys	Leu
			85					90						95	
Ser	Thr	Glu	Gln	Leu	Arg	Cys	Leu	Ala	His	Arg	Leu	Ser	Glu	Pro	Pro
		100						105					110		
Glu	Asp	Leu	Asp	Ala	Leu	Pro	Leu	Asp	Leu	Leu	Leu	Phe	Leu	Asn	Pro
	115						120					125			
Asp	Ala	Phe	Ser	Gly	Pro	Gln	Ala	Cys	Thr	Arg	Phe	Phe	Ser	Arg	Ile
	130					135					140				
Thr	Lys	Ala	Asn	Val	Asp	Leu	Leu	Pro	Arg	Gly	Ala	Pro	Glu	Arg	Gln
145					150					155					160
Arg	Leu	Leu	Pro	Ala	Ala	Leu	Ala	Cys	Trp	Gly	Val	Arg	Gly	Ser	Leu
			165					170						175	
Leu	Ser	Glu	Ala	Asp	Val	Arg	Ala	Leu	Gly	Gly	Leu	Ala	Cys	Asp	Leu
		180						185					190		
Pro	Gly	Arg	Phe	Val	Ala	Glu	Ser	Ala	Glu	Val	Leu	Leu	Pro	Arg	Leu
	195						200					205			
Val	Ser	Cys	Pro	Gly	Pro	Leu	Asp	Gln	Asp	Gln	Gln	Glu	Ala	Ala	Arg
	210					215				220					
Ala	Ala	Leu	Gln	Gly	Gly	Gly	Pro	Pro	Tyr	Gly	Pro	Pro	Ser	Thr	Trp
225				230						235					240
Ser	Val	Ser	Thr	Met	Asp	Ala	Leu	Arg	Gly	Leu	Leu	Pro	Val	Leu	Gly
			245						250					255	
Gln	Pro	Ile	Ile	Arg	Ser	Ile	Pro	Gln	Gly	Ile	Val	Ala	Ala	Trp	Arg
		260						265					270		
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile
	275					280						285			
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser
	290					295					300				
Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys
305					310					315					320
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met
			325					330						335	
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu
		340						345					350		
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val
		355					360					365			
Ile	Gln	His	Leu	Gly	Tyr	Leu	Phe	Leu	Lys	Met	Ser	Pro	Glu	Asp	Ile
	370					375					380				
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu
385					390					395					400
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Ala	Pro	Arg	Arg	Pro	Leu
			405						410					415	

Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln  
 420 425 430  
 Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr  
 435 440 445  
 Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser  
 450 455 460  
 Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln  
 465 470 475 480  
 Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn  
 485 490 495  
 Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro  
 500 505 510  
 Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu  
 515 520 525  
 Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val  
 530 535 540  
 Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala  
 545 550 555 560  
 Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln  
 565 570 575  
 Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
 580 585 590  
 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln  
 595 600 605  
 Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser  
 610 615 620  
 His Pro Ser Leu Cys Arg Gly Pro Leu Gly Asp Ala Leu Pro Pro Arg  
 625 630 635 640  
 Thr Trp Thr Cys Ser His Arg Pro Gly Thr Ala Pro Ser Leu His Pro  
 645 650 655  
 Gly Leu Arg Ala Pro Leu Pro Cys Trp Pro Gln Pro Cys Trp Gly Ser  
 660 665 670  
 Pro Pro Gly Gln Glu Gln Ala Arg Val Ile Pro Val Pro Pro Gln Glu  
 675 680 685  
 Asn Ser Arg Ser Val Asn Gly Asn Met Pro Pro Ala Asp Thr  
 690 695 700

&lt;210&gt; 194

&lt;211&gt; 2135

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 194

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&lt;210&gt; 195

&lt;211&gt; 630

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 195

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100         105         110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115         120         125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130         135         140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145         150         155         160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165         170         175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180         185         190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195         200         205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210         215         220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp

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200

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	260		265			270
Gln Arg Ser Ser Arg	Asp Pro Ser Trp Arg	Gln Pro Glu Arg	Thr Ile			
	275		280			285
Leu Arg Pro Arg Phe	Arg Arg Glu Val	Glu Lys Thr Ala	Cys Pro Ser			
	290		295			300
Gly Lys Lys Ala Arg	Glu Ile Asp Glu Ser	Leu Ile Phe Tyr	Lys Lys			
305		310		315		320
Trp Glu Leu Glu Ala	Cys Val Asp Ala Ala	Leu Leu Ala Thr	Gln Met			
	325		330			335
Asp Arg Val Asn Ala	Ile Pro Phe Thr Tyr	Glu Gln Leu Asp	Val Leu			
	340		345			350
Lys His Lys Leu Asp	Glu Leu Tyr Pro	Gln Gly Tyr Pro	Glu Ser Val			
	355		360			365
Ile Gln His Leu Gly	Tyr Leu Phe Leu Lys	Met Ser Pro Glu	Asp Ile			
	370		375			380
Arg Lys Trp Asn Val	Thr Ser Leu Glu Thr	Leu Lys Ala Leu	Leu Glu			
385		390		395		400
Val Asn Lys Gly His	Glu Met Ser Pro	Gln Ala Pro Arg	Arg Pro Leu			
	405		410			415
Pro Gln Val Ala Thr	Leu Ile Asp Arg	Phe Val Lys Gly	Arg Gly Gln			
	420		425			430
Leu Asp Lys Asp Thr	Leu Asp Thr Leu Thr	Ala Phe Tyr Pro	Gly Tyr			
	435		440			445
Leu Cys Ser Leu Ser	Pro Glu Leu Ser Ser	Val Pro Pro Ser	Ser Ser			
	450		455			460
Ile Trp Ala Val Arg	Pro Gln Asp Leu Asp	Thr Cys Asp Pro	Arg Gln			
465		470		475		480
Leu Asp Val Leu Tyr	Pro Lys Ala Arg	Leu Ala Phe Gln	Asn Met Asn			
	485		490			495
Gly Ser Glu Tyr Phe	Val Lys Ile Gln Ser	Phe Leu Gly Gly	Ala Pro			
	500		505			510
Thr Glu Asp Leu Lys	Ala Leu Ser Gln Gln	Asn Val Ser Met	Asp Leu			
	515		520			525
Ala Thr Phe Met Lys	Leu Arg Thr Asp	Ala Val Leu Pro	Leu Thr Val			
	530		535			540
Ala Glu Val Gln Lys	Leu Leu Gly Pro	His Val Glu Gly	Leu Lys Ala			
545		550		555		560
Glu Glu Arg His Arg	Pro Val Arg Asp	Trp Ile Leu Arg	Gln Arg Gln			
	565		570			575
Asp Asp Leu Asp Thr	Leu Gly Leu Gly	Leu Gln Gly Gly	Ile Pro Asn			
	580		585			590
Gly Tyr Leu Val Leu	Asp Leu Ser Val	Gln Glu Ala Leu	Ser Gly Thr			
	595		600			605
Pro Cys Leu Leu Gly	Pro Gly Pro Val	Leu Thr Val Leu	Ala Leu Leu			
	610		615			620
Leu Ala Ser Thr Leu	Ala					
625		630				

&lt;210&gt; 196

&lt;211&gt; 2105

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 196

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ggccggccac tcccgctctgc tgtgacgcgc ggacagagag ctaccgggtgg acccacggtg 60
cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctgttgggg 120
tctgtgggga ccccgccct cggcagcctc ctgttctctgc tcttcagcct cggatgggtg 180
cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
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gcgagggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360
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cccaggagacc tggacgcctt cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
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gtgcgggggt ctctgctgag cgaggctgat gtgctggctc tgggaggcct ggcttgcgac 660
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cggcaacgct cctctcgggg cccatcctgg cggcagcctg aacggaccat cctccggccg 960
cggttccggc gggaagtggg gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080
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ctcagccccg aggagctgag ctccgtgccc cccagcagca tctggggcgt caggccccag 1500
gacctggaca cgtgtgaccc aaggcagctg gacgtcctct atcccaaggc ccgccttgtc 1560
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aacggctacc tggctcctaga cctcagcgtg caaggacctg gacctgttct caccgtcctg 1920
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actcgcgctc agtaaacggg aacatgcccc ctgcagacac gtaaaaaaaaa aaaaaaaaaa 2100
aaaaa . 2105

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&lt;210&gt; 197

&lt;211&gt; 620

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 197

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100          105          110

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Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro  
 115 120 125  
 Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile  
 130 135 140  
 Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln  
 145 150 155 160  
 Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu  
 165 170 175  
 Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu  
 180 185 190  
 Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu  
 195 200 205  
 Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg  
 210 215 220  
 Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp  
 225 230 235 240  
 Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly  
 245 250 255  
 Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg  
 260 265 270  
 Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile  
 275 280 285  
 Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser  
 290 295 300  
 Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys  
 305 310 315 320  
 Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met  
 325 330 335  
 Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu  
 340 345 350  
 Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val  
 355 360 365  
 Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile  
 370 375 380  
 Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu  
 385 390 395 400  
 Val Asn Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu  
 405 410 415  
 Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln  
 420 425 430  
 Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr  
 435 440 445  
 Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser  
 450 455 460  
 Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln  
 465 470 475 480  
 Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn  
 485 490 495  
 Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro  
 500 505 510  
 Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu  
 515 520 525  
 Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val  
 530 535 540  
 Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala  
 545 550 555 560  
 Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln  
 565 570 575

203

Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
 580 585 590  
 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Pro Gly Pro Val Leu  
 595 600 605  
 Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala  
 610 615 620

&lt;210&gt; 198

&lt;211&gt; 2193

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 198

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cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctgttgggg 120
tcctgtggga ccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
ctggccaacc cacctaaccat ttccagcctc tcccctcgcc aactccttgg cttcccgtgt 300
gcgagggtgt ccggcctgag cacggagcgt gtcgggagc tggctgtggc cttggcacag 360
aagaatgtca agctctcaac agagcagctg cgctgtctgg ctacccggt cctctgagccc 420
cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaacc agatgcgttc 480
tcggggcccc aggcctgcac ccgtttcttc tcccgcatca cgaaggccaa tgtggacctg 540
ctcccgaggg gggctcccga gcgacagcgg ctgctgcctg cggctctggc ctgctggggt 600
gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660
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ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780
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cggcaacgct cctctcgga cccatcctgg cggcagcctg aacggaccat cctccggccg 960
cggttccggc ggggaagtga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
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gcagacacgt aaaaaaaaaa aaaaaaaaaa aaa 2193

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&lt;210&gt; 199

&lt;211&gt; 694

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 199

204

Met	Ala	Leu	Pro	Thr	Ala	Arg	Pro	Leu	Leu	Gly	Ser	Cys	Gly	Thr	Pro	1	5	10	15
Ala	Leu	Gly	Ser	Leu	Leu	Phe	Leu	Leu	Phe	Ser	Leu	Gly	Trp	Val	Gln	20	25	30	
Pro	Ser	Arg	Thr	Leu	Ala	Gly	Glu	Thr	Gly	Gln	Glu	Ala	Ala	Pro	Leu	35	40	45	
Asp	Gly	Val	Leu	Ala	Asn	Pro	Pro	Asn	Ile	Ser	Ser	Leu	Ser	Pro	Arg	50	55	60	
Gln	Leu	Leu	Gly	Phe	Pro	Cys	Ala	Glu	Val	Ser	Gly	Leu	Ser	Thr	Glu	65	70	75	80
Arg	Val	Arg	Glu	Leu	Ala	Val	Ala	Leu	Ala	Gln	Lys	Asn	Val	Lys	Leu	85	90	95	
Ser	Thr	Glu	Gln	Leu	Arg	Cys	Leu	Ala	His	Arg	Leu	Ser	Glu	Pro	Pro	100	105	110	
Glu	Asp	Leu	Asp	Ala	Leu	Pro	Leu	Asp	Leu	Leu	Leu	Phe	Leu	Asn	Pro	115	120	125	
Asp	Ala	Phe	Ser	Gly	Pro	Gln	Ala	Cys	Thr	Arg	Phe	Phe	Ser	Arg	Ile	130	135	140	
Thr	Lys	Ala	Asn	Val	Asp	Leu	Leu	Pro	Arg	Gly	Ala	Pro	Glu	Arg	Gln	145	150	155	160
Arg	Leu	Leu	Pro	Ala	Ala	Leu	Ala	Cys	Trp	Gly	Val	Arg	Gly	Ser	Leu	165	170	175	
Leu	Ser	Glu	Ala	Asp	Val	Arg	Ala	Leu	Gly	Gly	Leu	Ala	Cys	Asp	Leu	180	185	190	
Pro	Gly	Arg	Phe	Val	Ala	Glu	Ser	Ala	Glu	Val	Leu	Leu	Pro	Arg	Leu	195	200	205	
Val	Ser	Cys	Pro	Gly	Pro	Leu	Asp	Gln	Asp	Gln	Gln	Glu	Ala	Ala	Arg	210	215	220	
Ala	Ala	Leu	Gln	Gly	Gly	Gly	Pro	Pro	Tyr	Gly	Pro	Pro	Ser	Thr	Trp	225	230	235	240
Ser	Val	Ser	Thr	Met	Asp	Ala	Leu	Arg	Gly	Leu	Leu	Pro	Val	Leu	Gly	245	250	255	
Gln	Pro	Ile	Ile	Arg	Ser	Ile	Pro	Gln	Gly	Ile	Val	Ala	Ala	Trp	Arg	260	265	270	
Gln	Arg	Ser	Ser	Arg	Asp	Pro	Ser	Trp	Arg	Gln	Pro	Glu	Arg	Thr	Ile	275	280	285	
Leu	Arg	Pro	Arg	Phe	Arg	Arg	Glu	Val	Glu	Lys	Thr	Ala	Cys	Pro	Ser	290	295	300	
Gly	Lys	Lys	Ala	Arg	Glu	Ile	Asp	Glu	Ser	Leu	Ile	Phe	Tyr	Lys	Lys	305	310	315	320
Trp	Glu	Leu	Glu	Ala	Cys	Val	Asp	Ala	Ala	Leu	Leu	Ala	Thr	Gln	Met	325	330	335	
Asp	Arg	Val	Asn	Ala	Ile	Pro	Phe	Thr	Tyr	Glu	Gln	Leu	Asp	Val	Leu	340	345	350	
Lys	His	Lys	Leu	Asp	Glu	Leu	Tyr	Pro	Gln	Gly	Tyr	Pro	Glu	Ser	Val	355	360	365	
Ile	Gln	His	Leu	Gly	Tyr	Leu	Phe	Leu	Lys	Met	Ser	Pro	Glu	Asp	Ile	370	375	380	
Arg	Lys	Trp	Asn	Val	Thr	Ser	Leu	Glu	Thr	Leu	Lys	Ala	Leu	Leu	Glu	385	390	395	400
Val	Asn	Lys	Gly	His	Glu	Met	Ser	Pro	Gln	Val	Ala	Thr	Leu	Ile	Asp	405	410	415	
Arg	Phe	Val	Lys	Gly	Arg	Gly	Gln	Leu	Asp	Lys	Asp	Thr	Leu	Asp	Thr	420	425	430	
Leu	Thr	Ala	Phe	Tyr	Pro	Gly	Tyr	Leu	Cys	Ser	Leu	Ser	Pro	Glu	Glu	435	440	445	
Leu	Ser	Ser	Val	Pro	Pro	Ser	Ser	Ile	Trp	Ala	Val	Arg	Pro	Gln	Asp	450	455	460	



Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala  
 465 470 475 480  
 Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile  
 485 490 495  
 Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser  
 500 505 510  
 Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr  
 515 520 525  
 Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly  
 530 535 540  
 Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg  
 545 550 555 560  
 Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu  
 565 570 575  
 Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser  
 580 585 590  
 Val Gln Gly Gly Arg Gly Gly Gln Ala Arg Ala Gly Gly Arg Ala Gly  
 595 600 605  
 Gly Val Glu Val Gly Ala Leu Ser His Pro Ser Leu Cys Arg Gly Pro  
 610 615 620  
 Leu Gly Asp Ala Leu Pro Pro Arg Thr Trp Thr Cys Ser His Arg Pro  
 625 630 635 640  
 Gly Thr Ala Pro Ser Leu His Pro Gly Leu Arg Ala Pro Leu Pro Cys  
 645 650 655  
 Trp Pro Gln Pro Cys Trp Gly Ser Pro Pro Gly Gln Glu Gln Ala Arg  
 660 665 670  
 Val Ile Pro Val Pro Pro Gln Glu Asn Ser Arg Ser Val Asn Gly Asn  
 675 680 685  
 Met Pro Pro Ala Asp Thr  
 690

&lt;210&gt; 200

&lt;211&gt; 2081

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 200

ggccggccac tcccgtctgc tgtgacgcgc ggacagagag ctaccggtgg acccacggtg 60  
 cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctgttgggg 120  
 tctgtggga ccccgccct cggcagcctc ctgttctctgc tcttcagcct cggatgggtg 180  
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 gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360  
 aagaatgtca agctctcaac agagcagctg cgctgtctgg ctacccggct ctctgagccc 420  
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 ctgectgggc gctttgtggc cgagtgcggc gaagtgtctc taccgccggt ggtgagctgc 720  
 ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780  
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 gatgagagcc tcattctcta caagaagtgg gacttggaag cctgcgtgga tgcggccctg 1080  
 ctggccaccc atatggaccg cgtgaacgac atccccttca cctacgagca gctggacgtc 1140  
 ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200

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ctgggctacc tcttcctcaa gatgagccct gaggacattc gcaagtggaa tgtgacgtcc 1260
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gcctgagggc cccactccct tgctggcccc agccctgctg gggatccccg cctggccagg 1980
agcaggcacg ggtgatcccc gttccacccc aagagaactc gcgctcagta aacgggaaca 2040
tgccccctgc agacacgtaa aaaaaaaaaa aaaaaaaaaa a 2081

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&lt;210&gt; 201

&lt;211&gt; 612

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 201

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
  1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
  20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
  35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
  50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
  65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
  85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
  100         105         110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
  115         120         125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
  130         135         140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
  145         150         155         160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
  165         170         175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
  180         185         190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
  195         200         205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
  210         215         220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
  225         230         235         240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
  245         250         255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
  260         265         270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
  275         280         285

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207

Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser  
 290 295 300  
 Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys  
 305 310 315 320  
 Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met  
 325 330 335  
 Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu  
 340 345 350  
 Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val  
 355 360 365  
 Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile  
 370 375 380  
 Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu  
 385 390 395 400  
 Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp  
 405 410 415  
 Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr  
 420 425 430  
 Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu  
 435 440 445  
 Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp  
 450 455 460  
 Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala  
 465 470 475 480  
 Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile  
 485 490 495  
 Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser  
 500 505 510  
 Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr  
 515 520 525  
 Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly  
 530 535 540  
 Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg  
 545 550 555 560  
 Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu  
 565 570 575  
 Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser  
 580 585 590  
 Val Gln Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Leu Ala  
 595 600 605  
 Ser Thr Leu Ala  
 610

&lt;210&gt; 202

&lt;211&gt; 1195

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

gtggagaaga cagcctgtcc ttcaggcaag aaggcccgcg agatagacga gagcctcatc 60  
 ttctacaaga agtgggagct ggaagcctgc gtggatgcgg ccctgctggc caccagatg 120  
 gaccgcgtga acgccatccc cttcacctac gagcagctgg acgtcctaaa gcataaactg 180  
 gatgagctct acccacaagg ttaccccgag tctgtgatcc agcacctggg ctacctcttc 240  
 ctcaagatga gccctgagga cattcgcaag tggaatgtga cgtccctgga gaccctgaag 300  
 gctttgcttg aagtcaacaa agggcacgaa atgagtcctc aggtggccac cctgatcgac 360  
 cgctttgtga agggaagggg ccagctagac aaagacaccc tagacaccct gaccgccttc 420  
 taccctgggt acctgtgctc cctcagcccc gaggagctga gctccgtgcc cccagcagc 480

```

atctggggcg tcaggcccca ggacctggac acgtgtgacc caaggcagct ggacgtcctc 540
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cagtccttcc tgggtggggc cccacaggag gatttgaagg cgctcagtca gcagaatgtg 660
agcatggact tggccacgtt catgaagctg cggacggatg cgggtgctgcc gttgactgtg 720
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cggggcgggc aggccagggc tgggggcaga gctgggggcg tggaggtggg cgctctgagt 960
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&lt;210&gt; 203

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

```

Val Glu Lys Thr Ala Cys Pro Ser Gly Lys Lys Ala Arg Glu Ile Asp
 1          5          10          15
Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu Leu Glu Ala Cys Val Asp
          20          25          30
Ala Ala Leu Leu Ala Thr Gln Met Asp Arg Val Asn Ala Ile Pro Phe
          35          40          45
Thr Tyr Glu Gln Leu Asp Val Leu Lys His Lys Leu Asp Glu Leu Tyr
          50          55          60
Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln His Leu Gly Tyr Leu Phe
          65          70          75          80
Leu Lys Met Ser Pro Glu Asp Ile Arg Lys Trp Asn Val Thr Ser Leu
          85          90          95
Glu Thr Leu Lys Ala Leu Leu Glu Val Asn Lys Gly His Glu Met Ser
          100          105          110
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
          115          120          125
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
          130          135          140
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
          145          150          155          160
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
          165          170          175
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
          180          185          190
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
          195          200          205
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
          210          215          220
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
          225          230          235          240
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
          245          250          255
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
          260          265          270
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
          275          280          285
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln
          290          295          300
Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser

```

209

305		310		315		320
His Pro Ser Leu Cys Arg Gly Pro Leu Gly Asp Ala Leu Pro Pro Arg						
	325		330		335	
Thr Trp Thr Cys Ser His Arg Pro Gly Thr Ala Pro Ser Leu His Pro						
	340		345		350	
Gly Leu Arg Ala Pro Leu Pro Cys Trp Pro Gln Pro Cys Trp Gly Ser						
	355		360		365	
Pro Pro Gly Gln Glu Gln Ala Arg Val Ile Pro Val Pro Pro Gln Glu						
	370		375		380	
Asn Ser Arg Ser Val Asn Gly Asn Met Pro Pro Ala Asp Thr						
385	390		395			

<210> 204  
 <211> 2085  
 <212> DNA  
 <213> Homo sapiens

<400> 204

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ccctccctgg	gatctacaca	gaccatggcc	ttgccaacgg	ctcgaccctt	gttgggtgcc	120
tgtgggaccc	ccgccctcgg	cagcctcctg	ttcctgctct	tcagcctcgg	atgggtgcag	180
ccctcgagga	ccctggctgg	agagacaggg	caggaggctg	cacccttgga	cggagtcctg	240
gccaaccac	ctaacatttc	cagcctctcc	cctcgccaac	tccttggttt	cccgtgtgcg	300
gaggtgtccg	gcctgagcac	ggagcgtgtc	cgggagctgg	ctgtggcctt	ggcacagaag	360
aatgtcaagc	tctcaacaga	gcagctgcgc	tgtctggctc	accggtcttc	tgagccccc	420
gaggacctgg	acgccctccc	attggacctg	ctgctatttc	tcaaccacga	tgcgttctcg	480
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cctgggcgct	ttgtggccga	gtcggccgaa	gtgctgtctc	cccggctggg	gagctgccc	720
ggacccctgg	accaggacca	gcaggaggca	gccaggcg	ctctgcaggg	cgggggaccc	780
ccctacggcc	ccccgtcgac	atgggtctgtc	tccacgatgg	acgctctgcg	gggcctgctg	840
cccgtgctgg	gccagcccat	catccgcagc	atcccgcagg	gcctcgtggc	cgcgtggcgg	900
caacgctcct	ctcgggaccc	atcctggcgg	cagcctgaac	ggaccatcct	ccggccgcgg	960
ttccggcggg	aagtggagaa	gacagcctgt	ccttcaggca	agaaggcccc	cgagatagac	1020
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gccacccaga	tggaccgcgt	gaacgccatc	cccttcacct	acgagcagct	ggacgtccta	1140
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ccgttgactg	tggctgaggt	gcagaaactt	ctgggacccc	acgtggaggg	cctgaaggcg	1740
gaggagcggc	accgcccggg	gcgggactgg	atcctacggc	agcggcagga	cgacctggac	1800
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ctggcactgc	tcttagcctc	caccctggcc	tgaggggccc	actcccttgc	tgcccccagc	1980
cctgctgggg	atccccgcct	ggccaggagc	aggcacgggt	gatccccgtt	ccaccccaag	2040
agaactcgcg	ctcagtaaac	gggaacatgc	ccccctgcaga	cacgt		2085

<210> 205  
 <211> 622  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 205

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
 1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
          20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
          35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
          50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
          65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
          85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
          100          105          110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
          115          120          125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
          130          135          140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
          145          150          155          160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
          165          170          175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
          180          185          190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
          195          200          205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
          210          215          220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
          225          230          235          240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
          245          250          255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
          260          265          270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
          275          280          285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
          290          295          300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
          305          310          315          320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
          325          330          335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
          340          345          350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
          355          360          365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
          370          375          380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
          385          390          395          400
Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
          405          410          415
Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
          420          425          430
Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu

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211

435	440	445
Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp		
450	455	460
Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala		
465	470	475
Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile		
485	490	495
Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser		
500	505	510
Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr		
515	520	525
Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly		
530	535	540
Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg		
545	550	555
Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu		
565	570	575
Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser		
580	585	590
Val Gln Glu Ala Leu Ser Gly Thr Pro Cys Leu Leu Gly Pro Gly Pro		
595	600	605
Val Leu Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala		
610	615	620

&lt;210&gt; 206

&lt;211&gt; 2111

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 206

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cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctgttgggg 120
tcctgtggga ccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
cagccctcga ggacctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
ctggccaacc cacctaaccat ttccagcctc tcccctcgcc aactccttgg cttcccgtgt 300
gcgagggtgt ccggcctgag caccggagcgt gtccgggagc tggctgtggc cttggcacag 360
aagaatgtca agctctcaac agagcagctg cgctgtctgg ctcaccggct ctctgagccc 420
cccgaggacc tggtagccct cccattggac ctgctgctat tcctcaacc agatgcgttc 480
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ctcccgaggg gggtccccga gcgacagcgg ctgctgctg cggtcttggc ctgctggggg 600
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catctggacc tgccttatcc caaggcccgc cttgctttcc agaacatgaa cgggtccgaa 1560
tacttcgtga agatccagtc cttcctgggt ggggccccca cggaggattt gaaggcgctc 1620

```

212

```

agtcagcaga atgtgagcat ggacttggcc acgttcatga agctgcggac ggatgcggtg 1680
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agccctgctg gggatccccg cctggccagg agcaggcacg ggtgatcccc gttccacccc 2040
aagagaactc gcgtcagta aacgggaaca tgccccctgc agacacgtaa aaaaaaaaaa 2100
aaaaaaaaaa a 2111

```

&lt;210&gt; 207

&lt;211&gt; 2107

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

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tgcccgccca ctcccgctct ctgtgacgcg cggacagaga gctaccggtg gaccacaggt 60
gcctccctcc ctgggatcta cacagaccat ggccctgcaa cggtcgcacc cctgttggtc 120
ctgtggggac cgccctggca gcctcctgtt cctgctcttc agcctcggat ggggtgatcc 180
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aaccceccat aacatttcca gcctctcccc tcgccaactc cttggcttcc cgtgtgcgga 300
ggtgtccggc ctgagcacgg agcgtgtccg ggagctggct gtggccttg cacagaagaa 360
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gtgatccccg ttccaccca agagaactcg cgctcagtaa acgggaacat gccccctgca 2100
gacacgt 2107

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&lt;210&gt; 208

&lt;211&gt; 628

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;400&gt; 208

```

Met Ala Leu Gln Arg Leu Asp Pro Cys Trp Ser Cys Gly Asp Arg Pro
 1          5          10          15
Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val His Pro Ala
          20          25          30
Arg Thr Leu Ala Gly Glu Thr Gly Thr Glu Ser Ala Pro Leu Gly Gly
          35          40          45
Val Leu Thr Thr Pro His Asn Ile Ser Ser Leu Ser Pro Arg Gln Leu
          50          55          60
Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu Arg Val
65          70          75          80
Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu Ser Thr
          85          90          95
Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro Glu Asp
          100          105          110
Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro Asp Ala
          115          120          125
Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile Thr Lys
          130          135          140
Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln Arg Leu
145          150          155          160
Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu Leu Ser
          165          170          175
Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu Pro Gly
          180          185          190
Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu Val Ser
          195          200          205
Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg Ala Ala
          210          215          220
Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp Ser Val
225          230          235          240
Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly Gln Pro
          245          250          255
Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg Gln Arg
          260          265          270
Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile Leu Arg
          275          280          285
Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser Gly Lys
          290          295          300
Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu
305          310          315          320
Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met Asp Arg
          325          330          335
Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu Lys His
          340          345          350
Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln
          355          360          365
His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile Arg Lys
          370          375          380
Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu Val Asp
385          390          395          400
Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu Pro Gln
          405          410          415
Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln Leu Asp
          420          425          430
Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys
          435          440          445
Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser Ile Trp

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214

450	455	460
Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp		
465	470	475
Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn Gly Ser		480
	485	490
Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu		495
	500	505
Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu Ala Thr		510
	515	520
Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val Ala Glu		525
	530	535
Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala Glu Glu		540
545	550	555
Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp		560
	565	570
Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr		575
	580	585
Leu Val Leu Asp Leu Ser Val Gln Glu Thr Leu Ser Gly Thr Pro Cys		590
	595	600
Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Ala		605
	610	615
Ser Thr Leu Ala		620
625		

&lt;210&gt; 209

&lt;211&gt; 2316

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 209

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ctatagggag tgcacccacg cgtccgcccg gcgttagggg taaagctccc tacccaactg 60
cgcagaaggc ctcagaggcc tgggggctgg gcttcccctt tcacatcgcc ctttagaggc 120
ccacgtgtgg gcattggccs gcatctgtaa aggggctgtc ctgttcctca tgggcgctgc 180
cagcgccacg cactcctctt tctgcctggc cgccactcc cgtctgctgt gacgcgcgga 240
cagagagcta ccggtggacc caggtgacct ccctccctgg gatctacaca gaccatggcc 300
ttgccaacgg ctgcaccctt gttgggggtc tgtgggacct ccgcctcgg cagcctcctg 360
ttcctgctct tcagcctcgg atgggtgcag ccctcgagga ccctggctgg agagacaggg 420
caggaggctg cgcctctgga cggagtccct gccaacccac ctaacatttc cagcctctcc 480
cctcgccaac tccttggctt cccgtgtgct gaggtgtccg gcctgagcac ggagcgtgtc 540
cgggagctgg ctgtggcctt ggcacagaag aatgtcaagc tctcaacaga gcagctgcgc 600
tgtctggtc accggtctct tgagccccc gaggaacctg acgccctccc attggacctg 660
ctgtatttcc tyaacccaga tgcgttctcg gggcccagg cctgcacccg tttcttctcc 720
cgcatacaga aggccaatgt ggacctgtc ccgagggggg ctcccagagc acagcggctg 780
ctgacctgcg ctctggcctg ctgggggtgt cgggggtctc tgctgagcga ggctgatgtg 840
cgggctctgg gaggcctggc ttgcgacctg cctgggcgct ttgtggccga gtcggccgaa 900
gtgtgtctac cccggctggg gagctgcccc ggaccctgg accaggacca gcaggaggca 960
gccaggggcg ctctgcaggg cgggggacct ccctacggcc ccccgctcac atggtctgtc 1020
tccacgatgg acgctctgct gggcctgtct cccgtgtgtg gccagcccat catccgcagc 1080
atcccgagg gcactgtggc cgcgtggcgg caacgctcct ctccggacct atcctggcgg 1140
cagcctgaac ggaccatcct ccggcccgcg ttccggcggg aagtggagaa gacagcctgt 1200
ccttcaggca agaaggcccg cgagatagac gagagcctca tcttctacaa gaagtgggag 1260
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gggttaccgg agtctgtgat ccagcacctg ggtacctct tctcaagat gagccctgag 1440
gacattcgca agtggaatgt gacgtccctg gagaccctga aggttttct tgaagtcgac 1500
aaagggcacg aaatgagtc ttaggtcctt cggcgggccc tcccacaggt ggccacctg 1560
atcgaccgct ttgtgaaggg aaggggccag ctagacaaag acaccctaga caccctgacc 1620

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215

```

gccttctacc ctgggtacct gtgctccctc agccccgagg agctgagctc cgtgcccccc 1680
agcagcatct gggcggtcag gccccaggac ctggacacgt gtgacccaag gcagctggac 1740
gtcctctatc ccaaggcccg ccttgcttcc cagaacatga acgggtccga atacttcgtg 1800
aagatccagt ccttccctggg tggggccccc acggaggatt tgaaggcgct cagtcagcag 1860
aatgtgagca tggacttggc cacgttcatg aagctgcgga cggatgcggt gctgccgttg 1920
actgtggctg aggtgcagaa acttctggga cccacgtgg agggcctgaa ggcggaggag 1980
cggcaccgcc cgggtgcgga ctggatccta cggcagcggc aggacgacct ggacacgtg 2040
gggctggggc tacagggcgg catccccaac ggctacctgg tcctagacct cagcgtgcaa 2100
gasrccctct cggggacgcc ctgcctccta ggacctggac ctgttctcac cgtcctggca 2160
ctgctcctag cctccaccct ggctgaggg cccactccc ttgctggccc cagccctgct 2220
ggggatcccc gcctggccag gacgaggcac gggatgcc cgttccaccc caagagaact 2280
cgcgctcagt aaacgggaac atgcccctg cagaca 2316

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&lt;210&gt; 210

&lt;211&gt; 630

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(630)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 210

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
1          5          10          15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20          25          30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35          40          45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50          55          60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65          70          75          80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85          90          95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100         105         110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115         120         125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130         135         140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145         150         155         160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165         170         175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180         185         190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195         200         205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210         215         220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225         230         235         240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245         250         255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260         265         270

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216

Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile  
 275 280 285  
 Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser  
 290 295 300  
 Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys  
 305 310 315 320  
 Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met  
 325 330 335  
 Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu  
 340 345 350  
 Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val  
 355 360 365  
 Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile  
 370 375 380  
 Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu  
 385 390 395 400  
 Val Asp Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu  
 405 410 415  
 Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln  
 420 425 430  
 Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr  
 435 440 445  
 Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser  
 450 455 460  
 Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln  
 465 470 475 480  
 Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn  
 485 490 495  
 Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro  
 500 505 510  
 Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu  
 515 520 525  
 Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val  
 530 535 540  
 Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala  
 545 550 555 560  
 Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln  
 565 570 575  
 Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn  
 580 585 590  
 Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Xaa Xaa Leu Ser Gly Thr  
 595 600 605  
 Pro Cys Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu  
 610 615 620  
 Leu Ala Ser Thr Leu Ala  
 625 630

&lt;210&gt; 211

&lt;211&gt; 1721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 211

gaattccctg gctgcttgaa tctgttctgc cccctcccca cccatttcac caccaccatg 60  
 acaccgggca cccagtctcc tttcttctgc ctgctgctcc tcacagtgtc tacagttgtt 120  
 acaggttctg gtcattgcaag ctctacccca ggtggagaaa aggagacttc ggctaccag 180  
 agaagttcag tgccagctc tactgagaag aatgctgtga gtatgaccag cagcgtactc 240

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tccagccaca gccccggttc aggtctctcc accactcagg gacaggatgt cactctggcc 300
ccggccacgg aaccagcttc aggttcagct gccacctggg gacaggatgt cacctcggtc 360
ccagtaccca ggccagccct gggtccacc accccgccag cccacgatgt cacctcagcc 420
ccggacaaca agccagcccc gggtccacc gccccccag cccacggtgt cacctcggtc 480
ccggacacca ggccgcccc gggtccacc gccccccag cccacggtgt cacctcggtc 540
ccggacacca ggccgcccc gggtccacc gcgcccgcag cccacggtgt cacctcggtc 600
ccggacacca ggccgcccc gggtccacc gccccccag cccatggtgt cacctcggtc 660
ccggacaaca ggcccgctt gggtccacc gccctccag tccacaatgt cacctcggtc 720
tcaggctctg catcaggctc agcttctact ctggtgcaca acggcacctc tgccagggct 780
accacaaccc cagccagcaa gagcactcca ttctcaattc ccagccacca ctctgatact 840
cctaccacct ttgccagcca tagcaccaag actgatgcca gtagcactca ccatagcacg 900
gtacctctct tcacctctc caatcacagc acttctcccc agttgtctac tgggggtctc 960
ttctttttcc tgtcttttca catttcaaac ctccagttta attcctctct ggaagatccc 1020
agcaccgact actaccaaga gctgcagaga gacatttctg aaatgttttt gcagatttat 1080
aaacaagggg gttttctggg cctctccaat attaatgtta ggccaggatc tgtggtggta 1140
caattgactc tggccttcgg agaaggtacc atcaatgtcc acgacgtgga gacacagttc 1200
aatcagtata aaacggaagc agcctctcga tataacctga cgatctcaga cgtcagcggtg 1260
agtgatgtgc catttcttt ctctgccag tctggggctg ggggtgccagg ctggggcatc 1320
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gctgtctgtc agtgccgccc aaagaactac gggcagctgg acatctttcc agcccgggat 1440
acctaccatc ctatgagcga gtacccacc taccacacc atgggcgcta tgtgccccct 1500
agcagtaccg atcgtagccc ctatgagaag gtttctgcag gtaatggtgg cagcagcctc 1560
tcttacacaa acccagcagt ggcagccact tctgccaaact tgtaggggca cgtcgcctc 1620
tgagctgagt ggccagccag tgccattcca ctccactcag ggctctctgg gccagtcctc 1680
ctgggagccc ccaccacaac acttcccagg catggaattc c 1721

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&lt;210&gt; 212

&lt;211&gt; 515

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 212

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Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Thr
  1           5           10          15
Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
  20          25          30
Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
  35          40          45
Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
  50          55          60
Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln Asp Val Thr Leu
  65          70          75          80
Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
  85          90          95
Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
  100         105         110
Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
  115         120         125
Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
  130         135         140
Arg Pro Pro Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
  145         150         155         160
Ala Pro Asp Thr Arg Pro Pro Pro Gly Ser Thr Ala Pro Ala Ala His
  165         170         175
Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
  180         185         190
Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Asn Arg Pro Ala Leu
  195         200         205

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218

Ala Ser Thr Ala Pro Pro Val His Asn Val Thr Ser Ala Ser Gly Ser  
 210 215 220  
 Ala Ser Gly Ser Ala Ser Thr Leu Val His Asn Gly Thr Ser Ala Arg  
 225 230 235 240  
 Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe Ser Ile Pro Ser  
 245 250 255  
 His His Ser Asp Thr Pro Thr Thr Leu Ala Ser His Ser Thr Lys Thr  
 260 265 270  
 Asp Ala Ser Ser Thr His His Ser Thr Val Pro Pro Leu Thr Ser Ser  
 275 280 285  
 Asn His Ser Thr Ser Pro Gln Leu Ser Thr Gly Val Ser Phe Phe Phe  
 290 295 300  
 Leu Ser Phe His Ile Ser Asn Leu Gln Phe Asn Ser Ser Leu Glu Asp  
 305 310 315 320  
 Pro Ser Thr Asp Tyr Tyr Gln Glu Leu Gln Arg Asp Ile Ser Glu Met  
 325 330 335  
 Phe Leu Gln Ile Tyr Lys Gln Gly Gly Phe Leu Gly Leu Ser Asn Ile  
 340 345 350  
 Lys Phe Arg Pro Gly Ser Val Val Gln Leu Thr Leu Ala Phe Arg  
 355 360 365  
 Glu Gly Thr Ile Asn Val His Asp Val Glu Thr Gln Phe Asn Gln Tyr  
 370 375 380  
 Lys Thr Glu Ala Ala Ser Arg Tyr Asn Leu Thr Ile Ser Asp Val Ser  
 385 390 395 400  
 Val Ser Asp Val Pro Phe Pro Phe Ser Ala Gln Ser Gly Ala Gly Val  
 405 410 415  
 Pro Gly Trp Gly Ile Ala Leu Leu Val Leu Val Cys Val Leu Val Ala  
 420 425 430  
 Leu Ala Ile Val Tyr Leu Ile Ala Leu Ala Val Cys Gln Cys Arg Arg  
 435 440 445  
 Lys Asn Tyr Gly Gln Leu Asp Ile Phe Pro Ala Arg Asp Thr Tyr His  
 450 455 460  
 Pro Met Ser Glu Tyr Pro Thr Tyr His Thr His Gly Arg Tyr Val Pro  
 465 470 475 480  
 Pro Ser Ser Thr Asp Arg Ser Pro Tyr Glu Lys Val Ser Ala Gly Asn  
 485 490 495  
 Gly Gly Ser Ser Leu Ser Tyr Thr Asn Pro Ala Val Ala Ala Thr Ser  
 500 505 510  
 Ala Asn Leu  
 515

&lt;210&gt; 213

&lt;211&gt; 5793

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 213

cctggactgg acagagagcg gctatactgg gagctgagcc agctgaccaa cagcatcaca 60  
 gagctggggac cctacaccct ggatagggac agtctctatg tcaatggcct caacccttgg 120  
 agctctgtgc caaccaccag cactcctggg acctccacag tgcacctggc aacctctggg 180  
 actccatcct ccctgcctgg ccacacagcc cctgtccctc tcttgatacc attcaccctc 240  
 aactttacca tcaccaacct gcattatgaa gaaaacatgc aacaccctgg ttccaggaag 300  
 ttcaacacca cggagagggg tctgcagggt ctgctcaagc ccttggtcaa gagcaccagc 360  
 gttggccctc tgtactctgg ctgcagactg accttgctca gacctgagaa acatggggca 420  
 gccactggag tggagcccat ctgcaccctc cgccttgatc ccactgggtc tggactggac 480  
 agagagcggc tatactggga gctgagccag ctgaccaaca gcgttacaga gctggggccc 540  
 tacaccctgg acagggacag tctctatgtc aatggcttca cccatcggag ctctgtgcca 600

accaccagta	ttcctgggac	ctctgcagtg	cacctggaaa	cctctgggac	tccagcctcc	660
ctccctggcc	acacagcccc	tggccctctc	ctgggtgcat	tcaccctcaa	cttcactatc	720
accaacctgc	agtatgagga	ggacatgcgt	cacctgggtt	ccaggaagtt	caacaccacg	780
gagagagtcc	tgagggtct	gctcaagccc	ttgttcaaga	gcaccagtgt	tggccctctg	840
tactctggct	gcagactgac	cttgctcagg	cctgaaaaac	gtggggcagc	caccggcgctg	900
gacaccatct	gcactcaccg	ccttgaccct	ctaaaccctg	gactggacag	agagcagcta	960
tactgggagc	tgagcaaact	gacccgtggc	atcatcgagc	tgggccccta	cctcctggac	1020
agaggcagtc	tctatgtcaa	tggtttcacc	catcggaact	ttgtgcccac	caccagcact	1080
cctgggacct	ccacagtaca	cctaggaacc	tctgaaactc	catcctccct	acctagacct	1140
atagtgcctg	gccctctcct	ggtgccattc	accctcaact	tcaccatcac	caacttgacg	1200
tatgaggagc	ccatgacaga	ccctggctcc	aggaagttca	ataccacgga	gagggtccta	1260
cagggctctg	tcaggccctt	gttcaagaat	accagtatcg	gccctctgta	ctccagctgc	1320
agactgacct	tgctcaggcc	agagaaggac	aaggcagcca	ccagagtgga	tgccatctgt	1380
accaccacc	ctgaccctca	aagccctgga	ctgaacagag	agcagctgta	ctgggagctg	1440
agccagctga	cccacggcat	cactgagctg	ggcccctaca	ccctggacag	ggacagtctc	1500
tatgtcgatg	gtttcactca	ttggagcccc	ataccaacca	ccagcactcc	tgggacctcc	1560
atagtgaacc	tgggaacctc	tgggatccca	ccttccctcc	ctgaaactac	agccaccggc	1620
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gaccccaaaa	tccctgggct	agacagacag	cagctatact	gggagctgag	ccagctgacc	1920
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ttcaccacagc	ggagctctgt	gccaccacc	agcactcctg	ggactttcac	agtacagccg	2040
gaaacctctg	agactccatc	atccctccct	ggccccacag	ccactggccc	tgtcctgctg	2100
ccattcaccc	tcaattttac	catcattaac	ctgcagtatg	aggaggacat	gcacgcctcc	2160
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aaggatgggg	cagccaccag	agtggatgct	gtctgcaccc	atcgtcctga	ccccaaaagc	2340
cctggactgg	acagagagcg	gctgtactgg	aagctgagcc	agctgaccca	cggcatcact	2400
gagctggggc	cctacaccct	ggacaggcac	agtctctatg	tcaatggttt	cacccatcag	2460
agctctatga	cgaccaccag	aactcctgat	acctccacaa	tgacactggc	aacctcgaga	2520
actccagcct	ccctgtctgg	acctacgacc	gccagccctc	tccctgggtg	attcaccaatt	2580
aacttcacca	tcactaacct	gcggtatgag	gagaacatgc	atcaccctgg	ctctagaaag	2640
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gttgccctc	tgtactctgg	ctgcagactg	accttgctca	ggcccaagaa	ggatggggca	2760
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tacaccctgg	acagggacag	tctctatgtc	aatggtttca	cacagcggag	ctctgtgccc	2940
accactagca	ttcctgggac	ccccacagtg	gacctgggaa	catctgggac	tccagtttct	3000
aaacctggtc	cctcggctgc	cagccctctc	ctgggtctat	tcactctcaa	cttcaccatc	3060
accaacctgc	ggtatgagga	gaacatgcag	cacctgggct	ccaggaagtt	caacaccacg	3120
gagagggctc	ttcagggcct	gctcaggctc	ctgttcaaga	gcaccagtgt	tggccctctg	3180
tactctggct	gcagactgac	tttgcctcag	cctgaaaagg	atgggacagc	cactggagtg	3240
gatgccatct	gcaccaccca	ccctgacccc	aaaagcccta	ggctggacag	agagcagctg	3300
tattgggagc	tgagccagct	gaccacaaat	atcactgagc	tggggcacta	tggccctggac	3360
aacgacagcc	tctttgtcaa	tgggtttcact	catcggagct	ctgtgtccac	caccagcact	3420
cctgggaccc	ccacagtgtc	tctgggagca	tctaagactc	cagcctcgat	atgtggccct	3480
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220

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&lt;210&gt; 214

&lt;211&gt; 1783

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(1783)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 214

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 20           25           30
Tyr Val Asn Gly Phe Asn Pro Trp Ser Ser Val Pro Thr Thr Ser Thr
 35           40           45
Pro Gly Thr Ser Thr Val His Leu Ala Thr Ser Gly Thr Pro Ser Ser
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Leu Pro Gly His Thr Ala Pro Val Pro Leu Leu Ile Pro Phe Thr Leu
 65           70           75           80
Asn Phe Thr Ile Thr Asn Leu His Tyr Glu Glu Asn Met Gln His Pro
 85           90           95
Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
100          105          110
Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys
115          120          125
Arg Leu Thr Leu Leu Arg Pro Glu Lys His Gly Ala Ala Thr Gly Val

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Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly		175
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Phe Thr His Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Ser		190
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Ala Val His Leu Glu Thr Ser Gly Thr Pro Ala Ser Leu Pro Gly His		205
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Thr Ala Pro Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile		220
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Thr Asn Leu Gln Tyr Glu Glu Asp Met Arg His Pro Gly Ser Arg Lys		240
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Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Lys Pro Leu Phe		255
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Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu		270
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Leu Arg Pro Glu Lys Arg Gly Ala Ala Thr Gly Val Asp Thr Ile Cys		285
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Thr His Arg Leu Asp Pro Leu Asn Pro Gly Leu Asp Arg Glu Gln Leu		300
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Tyr Trp Glu Leu Ser Lys Leu Thr Arg Gly Ile Ile Glu Leu Gly Pro		320
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Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val Asn Gly Phe Thr His Arg		335
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Asn Phe Val Pro Ile Thr Ser Thr Pro Gly Thr Ser Thr Val His Leu		350
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Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro Arg Pro Ile Val Pro Gly		365
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Tyr Glu Glu Ala Met Arg His Pro Gly Ser Arg Lys Phe Asn Thr Thr		400
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Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr Ser		415
	420	425
Ile Gly Pro Leu Tyr Ser Ser Cys Arg Leu Thr Leu Leu Arg Pro Glu		430
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Lys Asp Lys Ala Ala Thr Arg Val Asp Ala Ile Cys Thr His His Pro		445
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Ser Gln Leu Thr His Gly Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp		480
	485	490
Arg Asp Ser Leu Tyr Val Asp Gly Phe Thr His Trp Ser Pro Ile Pro		495
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Thr Thr Ser Thr Pro Gly Thr Ser Ile Val Asn Leu Gly Thr Ser Gly		510
	515	520
Ile Pro Pro Ser Leu Pro Glu Thr Thr Ala Thr Gly Pro Leu Leu Val		525
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Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln Tyr Glu Glu Asn		540
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Met Gly His Pro Gly Ser Arg Lys Phe Asn Ile Thr Glu Ser Val Leu		560
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Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu		575
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Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Val		590

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Ala Thr Arg Val Asp Ala Ile Cys Thr His Arg Pro Asp Pro Lys Ile		
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His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu		640
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Tyr Val Asn Gly Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Thr		
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Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu		720
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Met Pro Leu Phe Lys Asn Thr Ser Val Ser Ser Leu Tyr Ser Gly Cys		
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Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Arg Val		
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Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp		780
	770	775
Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr		
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Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly		800
	805	810
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Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro		
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		845
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile		
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Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys		
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Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe		880
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		895
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu		
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Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys		
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Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu		
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Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro		
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Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg		960
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		975
Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Pro Thr Val Asp Leu		
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Gly Thr Ser Gly Thr Pro Val Ser Lys Pro Gly Pro Ser Ala Ala Ser		
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Pro Leu Leu Val Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Arg		
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Gln	Pro	Leu	Ser	Gly	Pro	Gly	Leu	Pro	Ile	Lys	Gln	Val	Phe	His	Glu		
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<213> Homo sapiens
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&lt;210&gt; 216

&lt;211&gt; 1148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

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Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Arg Val
 20          25          30
Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp
 35          40          45
Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr
 50          55          60
Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly
 65          70          75          80
Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr Pro Asp Thr Ser
 85          90          95
Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro
 100          105          110
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile
 115          120          125
Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys
 130          135          140
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe
 145          150          155          160
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
 165          170          175
Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys
 180          185          190
Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu
 195          200          205
Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro
 210          215          220
Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg

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Gly	Thr	Ser	Gly	Thr	Pro	Val	Ser	Lys	Pro	Gly	Pro	Ser	Ala	Ala	Ser
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Pro	Leu	Leu	Val	Leu	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Arg
			275					280					285		
Tyr	Glu	Glu	Asn	Met	Gln	His	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr
			290				295				300				
Glu	Arg	Val	Leu	Gln	Gly	Leu	Leu	Arg	Ser	Leu	Phe	Lys	Ser	Thr	Ser
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Val	Gly	Pro	Leu	Tyr	Ser	Gly	Cys	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu
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Lys	Asp	Gly	Thr	Ala	Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	His	Pro
			340					345					350		
Asp	Pro	Lys	Ser	Pro	Arg	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Trp	Glu	Leu
			355				360					365			
Ser	Gln	Leu	Thr	His	Asn	Ile	Thr	Glu	Leu	Gly	His	Tyr	Ala	Leu	Asp
					375						380				
Asn	Asp	Ser	Leu	Phe	Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Ser
385					390						395				400
Thr	Thr	Ser	Thr	Pro	Gly	Thr	Pro	Thr	Val	Tyr	Leu	Gly	Ala	Ser	Lys
				405							410			415	
Thr	Pro	Ala	Ser	Ile	Phe	Gly	Pro	Ser	Ala	Ala	Ser	His	Leu	Leu	Ile
			420					425					430		
Leu	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Arg	Tyr	Glu	Glu	Asn
			435				440					445			
Met	Trp	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr	Glu	Arg	Val	Leu	Gln
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Gly	Leu	Leu	Arg	Pro	Leu	Phe	Lys	Asn	Thr	Ser	Val	Gly	Pro	Leu	Tyr
465					470					475					480
Ser	Gly	Ser	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu	Lys	Asp	Gly	Glu	Ala
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Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	His	Arg	Pro	Asp	Pro	Thr	Gly	Pro
			500					505					510		
Gly	Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Leu	Glu	Leu	Ser	Gln	Leu	Thr	His
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Ser	Ile	Thr	Glu	Leu	Gly	Pro	Tyr	Thr	Leu	Asp	Arg	Asp	Ser	Leu	Tyr
					535					540					
Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Pro	Thr	Thr	Ser	Thr	Gly
545					550					555					560
Val	Val	Ser	Glu	Glu	Pro	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Asn	Asn	Leu
				565						570				575	
Arg	Tyr	Met	Ala	Asp	Met	Gly	Gln	Pro	Gly	Ser	Leu	Lys	Phe	Asn	Ile
			580					585							

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Ser Glu Ala Thr Thr	Ala Met Gly Tyr His	Leu Lys Thr Leu Thr Leu
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Asn Phe Thr Ile Ser	Asn Leu Gln Tyr Ser	Pro Asp Met Gly Lys Gly
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Ser Ala Thr Phe Asn	Ser Thr Glu Gly Val	Leu Gln His Leu Leu Arg
	740	745
Pro Leu Phe Gln Lys	Ser Ser Met Gly Pro	Phe Tyr Leu Gly Cys Gln
	755	760
Leu Ile Ser Leu Arg	Pro Glu Lys Asp Gly	Ala Ala Thr Gly Val Asp
	770	775
Thr Thr Cys Thr Tyr	His Pro Asp Pro	Val Gly Pro Gly Leu Asp Ile
	785	790
Gln Gln Leu Tyr Trp	Glu Leu Ser Gln	Leu Thr His Gly Val Thr Gln
	805	810
Leu Gly Phe Tyr Val	Leu Asp Arg Asp	Ser Leu Phe Ile Asn Gly Tyr
	820	825
Ala Pro Gln Asn Leu	Ser Ile Arg Gly	Glu Tyr Gln Ile Asn Phe His
	835	840
Ile Val Asn Trp Asn	Leu Ser Asn Pro	Asp Pro Thr Ser Ser Glu Tyr
	850	855
Ile Thr Leu Leu Arg	Asp Ile Gln Asp	Lys Val Thr Thr Leu Tyr Lys
	865	870
Gly Ser Gln Leu His	Asp Thr Phe Arg	Phe Cys Leu Val Thr Asn Leu
	885	890
Thr Met Asp Ser Val	Leu Val Thr Val	Lys Ala Leu Phe Ser Ser Asn
	900	905
Leu Asp Pro Ser Leu	Val Glu Gln Val	Phe Leu Asp Lys Thr Leu Asn
	915	920
Ala Ser Phe His Trp	Leu Gly Ser Thr	Tyr Gln Leu Val Asp Ile His
	930	935
Val Thr Glu Met Glu	Ser Ser Val Tyr	Gln Pro Thr Ser Ser Ser Ser
	945	950
Thr Gln His Phe Tyr	Pro Asn Phe Thr	Ile Thr Asn Leu Pro Tyr Ser
	965	970
Gln Asp Lys Ala Gln	Pro Gly Thr Thr	Asn Tyr Gln Arg Asn Lys Arg
	980	985
Asn Ile Glu Asp Ala	Leu Asn Gln Leu	Phe Arg Asn Ser Ser Ile Lys
	995	1000
Ser Tyr Phe Ser Asp	Cys Gln Val Ser	Thr Phe Arg Ser Val Pro Asn
	1010	1015
Arg His His Thr Gly	Val Asp Ser Leu	Cys Asn Phe Ser Pro Leu Ala
	1025	1030
Arg Arg Val Asp Arg	Val Ala Ile Tyr	Glu Gln Phe Leu Arg Met Thr
	1045	1050
Arg Asn Gly Thr Gln	Leu Gln Asn Phe	Thr Leu Asp Arg Ser Ser Val
	1060	1065
Leu Val Asp Gly Tyr	Ser Pro Asn Arg	Asn Glu Pro Leu Thr Gly Asn
	1075	1080
Ser Asp Leu Pro Phe	Trp Ala Val Ile	Phe Ile Gly Leu Ala Gly Leu
	1090	1095
Leu Gly Leu Ile Thr	Cys Leu Ile Cys	Gly Val Leu Val Thr Thr Arg
	1105	1110
Arg Arg Lys Lys Glu	Gly Glu Tyr Asn	Val Gln Gln Gln Cys Pro Gly
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Tyr Tyr Gln Ser His	Leu Asp Leu Glu	Asp Leu Gln
	1140	1145



<210> 217  
 <211> 1890  
 <212> PRT  
 <213> Homo sapiens

<400> 217

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Glu	Leu	Ser	Gln	Leu	Thr	Asn	Ser	Ile	Thr	Glu	Leu	Gly	Pro	Tyr	Thr
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Leu	Asp	Arg	Asp	Ser	Leu	Tyr	Val	Asn	Gly	Phe	Asn	Pro	Trp	Ser	Ser
		35					40					45			
Val	Pro	Thr	Thr	Ser	Thr	Pro	Gly	Thr	Ser	Thr	Val	His	Leu	Ala	Thr
	50					55					60				
Ser	Gly	Thr	Pro	Ser	Ser	Leu	Pro	Gly	His	Thr	Ala	Pro	Val	Pro	Leu
65					70					75					80
Leu	Ile	Pro	Phe	Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	His	Tyr	Glu
				85					90					95	
Glu	Asn	Met	Gln	His	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr	Glu	Arg
			100					105					110		
Val	Leu	Gln	Gly	Leu	Leu	Lys	Pro	Leu	Phe	Lys	Ser	Thr	Ser	Val	Gly
		115					120					125			
Pro	Leu	Tyr	Ser	Gly	Cys	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu	Lys	His
	130					135					140				
Gly	Ala	Ala	Thr	Gly	Val	Asp	Ala	Ile	Cys	Thr	Leu	Arg	Leu	Asp	Pro
145					150					155					160
Thr	Gly	Pro	Gly	Leu	Asp	Arg	Glu	Arg	Leu	Tyr	Trp	Glu	Leu	Ser	Gln
				165					170					175	
Leu	Thr	Asn	Ser	Val	Thr	Glu	Leu	Gly	Pro	Tyr	Thr	Leu	Asp	Arg	Asp
			180					185					190		
Ser	Leu	Tyr	Val	Asn	Gly	Phe	Thr	His	Arg	Ser	Ser	Val	Pro	Thr	Thr
	195						200					205			
Ser	Ile	Pro	Gly	Thr	Ser	Ala	Val	His	Leu	Glu	Thr	Ser	Gly	Thr	Pro
	210					215					220				
Ala	Ser	Leu	Pro	Gly	His	Thr	Ala	Pro	Gly	Pro	Leu	Leu	Val	Pro	Phe
225					230					235					240
Thr	Leu	Asn	Phe	Thr	Ile	Thr	Asn	Leu	Gln	Tyr	Glu	Glu	Asp	Met	Arg
				245					250					255	
His	Pro	Gly	Ser	Arg	Lys	Phe	Asn	Thr	Thr	Glu	Arg	Val	Leu	Gln	Gly
			260					265					270		
Leu	Leu	Lys	Pro	Leu	Phe	Lys	Ser	Thr	Ser	Val	Gly	Pro	Leu	Tyr	Ser
		275					280					285			
Gly	Cys	Arg	Leu	Thr	Leu	Leu	Arg	Pro	Glu	Lys	Arg	Gly	Ala	Ala	Thr
		290				295					300				
Gly	Val	Asp	Thr	Ile	Cys	Thr	His	Arg	Leu	Asp	Pro	Leu	Asn	Pro	Gly
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Leu	Asp	Arg	Glu	Gln	Leu	Tyr	Trp	Glu	Leu	Ser	Lys	Leu	Thr	Arg	Gly
				325					330					335	
Ile	Ile	Glu	Leu	Gly	Pro	Tyr	Leu	Leu	Asp	Arg	Gly	Ser	Leu	Tyr	Val
			340					345					350		
Asn	Gly	Phe	Thr	His	Arg	Asn	Phe	Val	Pro	Ile	Thr	Ser	Thr	Pro	Gly
		355					360					365			
Thr	Ser	Thr	Val	His	Leu	Gly	Thr	Ser	Glu	Thr	Pro	Ser	Ser	Leu	Pro
	370					375					380				
Arg	Pro	Ile	Val	Pro	Gly	Pro	Leu	Leu	Val	Pro	Phe	Thr	Leu	Asn	Phe
385					390					395					400
Thr	Ile	Thr	Asn	Leu	Gln	Tyr	Glu	Glu	Ala	Met	Arg	His	Pro	Gly	Ser



865		870		875		880
His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly						
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Leu Leu Arg Pro Val Phe Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser						
	900			905		910
Gly Cys Arg Leu Thr Leu Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr						
	915			920		925
Lys Val Asp Ala Ile Cys Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly						
	930			935		940
Leu Asp Arg Glu Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Ser						
945		950			955	960
Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val						
	965			970		975
Asn Gly Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly						
	980			985		990
Thr Pro Thr Val Asp Leu Gly Thr Ser Gly Thr Pro Val Ser Lys Pro						
	995			1000		1005
Gly Pro Ser Ala Ala Ser Pro Leu Leu Val Leu Phe Thr Leu Asn Phe						
	1010			1015		1020
Thr Ile Thr Asn Leu Arg Tyr Glu Glu Asn Met Gln His Pro Gly Ser						
1025		1030			1035	1040
Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Ser						
	1045			1050		1055
Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu						
	1060			1065		1070
Thr Leu Leu Arg Pro Glu Lys Asp Gly Thr Ala Thr Gly Val Asp Ala						
	1075			1080		1085
Ile Cys Thr His His Pro Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu						
	1090			1095		1100
Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Asn Ile Thr Glu Leu						
1105		1110			1115	1120
Gly Pro Tyr Ala Leu Asp Asn Asp Ser Leu Phe Val Asn Gly Phe Thr						
	1125			1130		1135
His Arg Ser Ser Val Ser Thr Thr Ser Thr Pro Gly Thr Pro Thr Val						
	1140			1145		1150
Tyr Leu Gly Ala Ser Lys Thr Pro Ala Ser Ile Phe Gly Pro Ser Ala						
	1155			1160		1165
Ala Ser His Leu Leu Ile Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn						
	1170			1175		1180
Leu Arg Tyr Glu Glu Asn Met Trp Pro Gly Ser Arg Lys Phe Asn Thr						
1185		1190			1195	1200
Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr						
	1205			1210		1215
Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro						
	1220			1225		1230
Glu Lys Asp Gly Glu Ala Thr Gly Val Asp Ala Ile Cys Thr His Arg						
	1235			1240		1245
Pro Asp Pro Thr Gly Pro Gly Leu Asp Arg Glu Gln Leu Tyr Leu Glu						
	1250			1255		1260
Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu						
1265		1270			1275	1280
Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr His Arg Ser Ser Val						
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Pro Thr Thr Ser Thr Gly Val Val Ser Glu Glu Pro Phe Thr Leu Asn						
	1300			1305		1310
Phe Thr Ile Asn Asn Leu Arg Tyr Met Ala Asp Met Gly Gln Pro Gly						
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Ser Leu Lys Phe Asn Ile Thr Asp Asn Val Met Gln His Leu Leu Ser						

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Pro Leu Phe Gln Arg Ser Ser Leu Gly Ala Arg Tyr Thr Gly Cys Arg		
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Val Ile Ala Leu Arg Ser Val Lys Asn Gly Ala Glu Thr Arg Val Asp		1360
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Leu Leu Cys Thr Tyr Leu Gln Pro Leu Ser Gly Pro Gly Leu Pro Ile		1375
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Lys Gln Val Phe His Glu Leu Ser Gln Gln Thr His Gly Ile Thr Arg		1390
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Leu Gly Pro Tyr Ser Leu Asp Lys Asp Ser Leu Tyr Leu Asn Gly Tyr		1405
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Asn Glu Pro Gly Pro Asp Glu Pro Pro Thr Thr Pro Lys Pro Ala Thr		1420
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Leu Lys Thr Leu Thr Leu Asn Phe Thr Ile Ser Asn Leu Gln Tyr Ser		1455
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Pro Asp Met Gly Lys Gly Ser Ala Thr Phe Asn Ser Thr Glu Gly Val		1470
	1475	1480
Leu Gln His Leu Leu Arg Pro Leu Phe Gln Lys Ser Ser Met Gly Pro		1485
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Phe Tyr Leu Gly Cys Gln Leu Ile Ser Leu Arg Pro Glu Lys Asp Gly		1500
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Ala Ala Thr Gly Val Asp Thr Thr Cys Thr Tyr His Pro Asp Pro Val		1520
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Gly Pro Gly Leu Asp Ile Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu		1535
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Thr His Gly Val Thr Gln Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser		1550
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Leu Phe Ile Asn Gly Tyr Ala Pro Gln Asn Leu Ser Ile Arg Gly Glu		1565
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Ala Leu Phe Ser Ser Asn Leu Asp Pro Ser Leu Val Glu Gln Val Phe		1645
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Leu Asp Lys Thr Leu Asn Ala Ser Phe His Trp Leu Gly Ser Thr Tyr		1660
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Gln Leu Val Asp Ile His Val Thr Glu Met Glu Ser Ser Val Tyr Gln		1680
	1685	1690
Pro Thr Ser Ser Ser Thr Gln His Phe Tyr Pro Asn Phe Thr Ile		1695
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Thr Asn Leu Pro Tyr Ser Gln Asp Lys Ala Gln Pro Gly Thr Thr Asn		1710
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Arg Asn Ser Ser Ile Lys Ser Tyr Phe Ser Asp Cys Gln Val Ser Thr		1740
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Asn Phe Ser Pro Leu Ala Arg Arg Val Asp Arg Val Ala Ile Tyr Glu		1775
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Glu Phe Leu Arg Met Thr Arg Asn Gly Thr Gln Leu Gln Asn Phe Thr		1790

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Glu Pro Leu Thr Gly Asn Ser Asp	Leu Pro Phe Trp Ala Val Ile Leu	
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Ile Gly Leu Ala Gly Leu Leu Gly	Leu Ile Thr Cys Leu Ile Cys Gly	1840
	1845	1850
Val Leu Val Thr Thr Arg Arg Arg	Lys Lys Glu Gly Glu Tyr Asn Val	1855
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Gln Gln Gln Cys Pro Gly Tyr Tyr	Gln Ser His Leu Asp Leu Glu Asp	1870
	1875	1880
Leu Gln		1885
1890		

&lt;210&gt; 218

&lt;211&gt; 4939

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

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tcaaaaaaaa aaaaaaaaaa

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&lt;210&gt; 219

&lt;211&gt; 1465

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 219

Met Ser Leu Val Thr Val Pro Phe Tyr Gln Lys Arg His Arg His Phe

1

5

10

15

Asp Gln Ser Tyr Arg Asn Ile Gln Thr Arg Tyr Leu Leu Asp Glu Tyr

20

25

30

Ala Ser Lys Lys Arg Ala Ser Thr Gln Ala Ser Ser Gln Lys Ser Leu

35					40					45					
Ser	Gln	Arg	Ser	Ser	Ser	Gln	Arg	Ala	Ser	Ser	Gln	Thr	Ser	Leu	Gly
50						55					60				
Gly	Thr	Ile	Cys	Arg	Val	Cys	Ala	Lys	Arg	Val	Ser	Thr	Gln	Glu	Asp
65					70					75					80
Glu	Glu	Gln	Glu	Asn	Arg	Ser	Arg	Tyr	Gln	Ser	Leu	Val	Ala	Ala	Tyr
				85					90					95	
Gly	Glu	Ala	Lys	Arg	His	Gly	Phe	Leu	Ser	Glu	Leu	Ala	His	Leu	Glu
			100					105					110		
Glu	Asp	Val	His	Leu	Ala	Arg	Ser	Gln	Ala	Arg	Asp	Lys	Leu	Asp	Lys
	115					120						125			
Tyr	Ala	Ile	Gln	Gln	Met	Met	Glu	Asp	Lys	Leu	Ala	Trp	Glu	Arg	His
130					135					140					
Thr	Phe	Glu	Glu	Arg	Ile	Ser	Arg	Ala	Pro	Glu	Ile	Leu	Val	Arg	Leu
145					150					155					160
Arg	Ser	His	Thr	Val	Trp	Glu	Arg	Met	Ser	Val	Lys	Leu	Cys	Phe	Thr
				165					170					175	
Val	Gln	Gly	Phe	Pro	Thr	Pro	Val	Val	Gln	Trp	Tyr	Lys	Asp	Gly	Ser
			180					185					190		
Leu	Ile	Cys	Gln	Ala	Ala	Glu	Pro	Gly	Lys	Tyr	Arg	Ile	Glu	Ser	Asn
	195					200						205			
Tyr	Gly	Val	His	Thr	Leu	Glu	Ile	Asn	Arg	Ala	Asp	Phe	Asp	Asp	Thr
210					215						220				
Ala	Thr	Tyr	Ser	Ala	Val	Ala	Thr	Asn	Ala	His	Gly	Gln	Val	Ser	Thr
225					230					235					240
Asn	Ala	Ala	Val	Val	Val	Arg	Arg	Phe	Arg	Gly	Asp	Glu	Glu	Pro	Phe
				245					250					255	
Arg	Ser	Val	Gly	Leu	Pro	Ile	Gly	Leu	Pro	Leu	Ser	Ser	Met	Ile	Pro
			260					265					270		
Tyr	Thr	His	Phe	Asp	Val	Gln	Phe	Leu	Glu	Lys	Phe	Gly	Val	Thr	Phe
	275					280						285			
Arg	Arg	Glu	Gly	Glu	Thr	Val	Thr	Leu	Lys	Cys	Thr	Met	Leu	Val	Thr
290					295						300				
Pro	Asp	Leu	Lys	Arg	Val	Gln	Pro	Arg	Ala	Glu	Trp	Tyr	Arg	Asp	Asp
305					310					315					320
Leu	Leu	Leu	Lys	Glu	Ser	Lys	Trp	Thr	Lys	Met	Phe	Phe	Gly	Glu	Gly
				325					330					335	
Gln	Ala	Ser	Leu	Ser	Phe	Ser	His	Leu	His	Lys	Asp	Asp	Glu	Gly	Leu
			340					345					350		
Tyr	Thr	Leu	Arg	Ile	Val	Ser	Arg	Gly	Gly	Val	Thr	Asp	His	Ser	Ala
	355					360						365			
Phe	Leu	Phe	Val	Arg	Asp	Ala	Asp	Pro	Leu	Val	Thr	Gly	Ala	Pro	Gly
370					375						380				
Ala	Pro	Met	Asp	Leu	Gln	Cys	His	Asp	Ala	Asn	Arg	Asp	Tyr	Val	Ile
385					390					395					400
Val	Thr	Trp	Lys	Pro	Pro	Asn	Thr	Thr	Thr	Glu	Ser	Pro	Val	Met	Gly
				405					410					415	
Tyr	Phe	Val	Asp	Arg	Cys	Glu	Val	Gly	Thr	Asn	Asn	Trp	Val	Gln	Cys
			420					425					430		
Asn	Asp	Ala	Pro	Val	Lys	Ile	Cys	Lys	Tyr	Pro	Val	Thr	Gly	Leu	Phe
	435					440						445			
Glu	Gly	Arg	Ser	Tyr	Ile	Phe	Arg	Val	Arg	Ala	Val	Asn	Ser	Ala	Gly
450					455					460					
Ile	Ser	Arg	Pro	Ser	Arg	Val	Ser	Asp	Ala	Val	Ala	Ala	Leu	Asp	Pro
465					470					475					480
Leu	Asp	Leu	Arg	Arg	Leu	Gln	Ala	Val	His	Leu	Glu	Gly	Glu	Lys	Glu
				485					490					495	
Ile	Ala	Ile	Tyr	Gln	Asp	Asp	Leu	Glu	Gly	Asp	Ala	Gln	Val	Pro	Gly





Leu	Gly	Thr	Tyr	Ser	Val	Ser	Val	Ser	Asp	Thr	Asp	Gly	Val	Ser	Ser	
			980						985				990			
Ser	Phe	Val	Leu	Asp	Pro	Glu	Glu	Leu	Glu	Arg	Leu	Met	Ala	Leu	Ser	
		995					1000					1005				
Asn	Glu	Ile	Lys	Asn	Pro	Thr	Ile	Pro	Leu	Lys	Ser	Glu	Leu	Ala	Tyr	
	1010					1015					1020					
Glu	Ile	Phe	Asp	Lys	Gly	Arg	Val	Arg	Phe	Trp	Leu	Gln	Ala	Glu	His	
1025						1030				1035					1040	
Leu	Ser	Pro	Asp	Ala	Ser	Tyr	Arg	Phe	Ile	Ile	Asn	Asp	Arg	Glu	Val	
				1045					1050						1055	
Ser	Asp	Ser	Glu	Ile	His	Arg	Ile	Lys	Cys	Asp	Lys	Ala	Thr	Gly	Ile	
			1060					1065					1070			
Ile	Glu	Met	Val	Met	Asp	Arg	Phe	Ser	Ile	Glu	Asn	Glu	Gly	Thr	Tyr	
		1075					1080					1085				
Thr	Val	Gln	Ile	His	Asp	Gly	Lys	Ala	Lys	Ser	Gln	Ser	Ser	Leu	Val	
	1090					1095					1100					
Leu	Ile	Gly	Asp	Ala	Phe	Lys	Thr	Val	Leu	Glu	Glu	Ala	Glu	Phe	Gln	
1105						1110				1115					1120	
Arg	Lys	Glu	Phe	Leu	Arg	Lys	Gln	Gly	Pro	His	Phe	Ala	Glu	Tyr	Leu	
				1125					1130						1135	
His	Trp	Asp	Val	Thr	Glu	Glu	Cys	Glu	Val	Arg	Leu	Val	Cys	Lys	Val	
			1140					1145					1150			
Ala	Asn	Thr	Lys	Lys	Glu	Thr	Val	Phe	Lys	Trp	Leu	Lys	Asp	Asp	Ala	
		1155					1160					1165				
Leu	Tyr	Glu	Thr	Glu	Thr	Leu	Pro	Asn	Leu	Glu	Arg	Gly	Ile	Cys	Glu	
	1170					1175					1180					
Leu	Leu	Ile	Pro	Lys	Leu	Ser	Lys	Lys	Asp	His	Gly	Glu	Tyr	Lys	Ala	
1185						1190				1195					1200	
Thr	Leu	Lys	Asp	Asp	Arg	Gly	Gln	Asp	Val	Ser	Ile	Leu	Glu	Ile	Ala	
				1205					1210						1215	
Gly	Lys	Val	Tyr	Asp	Asp	Met	Ile	Leu	Ala	Met	Ser	Arg	Val	Cys	Gly	
			1220					1225					1230			
Lys	Ser	Ala	Ser	Pro	Leu	Lys	Val	Leu	Cys	Thr	Pro	Glu	Gly	Ile	Arg	
		1235					1240					1245				
Leu	Gln	Cys	Phe	Met	Lys	Tyr	Phe	Thr	Asp	Glu	Met	Lys	Val	Asn	Trp	
	1250					1255					1260					
Cys	His	Lys	Asp	Ala	Lys	Ile	Ser	Ser	Ser	Glu	His	Met	Arg	Ile	Gly	
1265						1270				1275					1280	
Gly	Ser	Glu	Glu	Met	Ala	Trp	Leu	Gln	Ile	Cys	Glu	Pro	Thr	Glu	Lys	
				1285					1290						1295	
Asp	Lys</															

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1425                                      1430                                      1435                                      1440  
 Lys Ile Pro Asp Met Ala Pro Pro Gln Gln Ala Lys Pro Lys Leu Ile  
    1445                                      1450                                      1455  
 Pro Ala Ser Ala Ser Ala Ala Gly Gln  
    1460                                      1465

&lt;210&gt; 220

&lt;211&gt; 4135

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 220

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&lt;210&gt; 221

&lt;211&gt; 689

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 221

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Met Ala Pro Trp Pro Glu Leu Gly Asp Ala Gln Pro Asn Pro Asp Lys
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Tyr Leu Glu Gly Ala Ala Gly Gln Gln Pro Thr Ala Pro Asp Lys Ser
20          25          30
Lys Glu Thr Asn Lys Asn Asn Thr Glu Ala Pro Val Thr Lys Ile Glu
35          40          45
Leu Leu Pro Ser Tyr Ser Thr Ala Thr Leu Ile Asp Glu Pro Thr Glu
50          55          60
Val Asp Asp Pro Trp Asn Leu Pro Thr Leu Gln Asp Ser Gly Ile Lys
65          70          75          80
Trp Ser Glu Arg Asp Thr Lys Gly Lys Ile Leu Cys Phe Phe Gln Gly
85          90          95
Ile Gly Arg Leu Ile Leu Leu Leu Gly Phe Leu Tyr Phe Phe Val Cys
100          105          110
Ser Leu Asp Ile Leu Ser Ser Ala Phe Gln Leu Val Gly Gly Lys Met
115          120          125
Ala Gly Gln Phe Phe Ser Asn Ser Ser Ile Met Ser Asn Pro Leu Leu
130          135          140
Gly Leu Val Ile Gly Val Leu Val Thr Val Leu Val Gln Ser Ser Ser
145          150          155          160
Thr Ser Thr Ser Ile Val Val Ser Met Val Ser Ser Ser Leu Leu Thr
165          170          175
Val Arg Ala Ala Ile Pro Ile Ile Met Gly Ala Asn Ile Gly Thr Ser
180          185          190
Ile Thr Asn Thr Ile Val Ala Leu Met Gln Val Gly Asp Arg Ser Glu
195          200          205
Phe Arg Arg Ala Phe Ala Gly Ala Thr Val His Asp Phe Phe Asn Trp

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240

210		215		220	
Leu Ser Leu Leu Val	Leu Leu Pro Val Glu Val	Ala Thr His Tyr Leu			
225	230	235	240		
Glu Ile Ile Thr Gln	Leu Ile Val Glu Ser Phe	His Phe Lys Asn Gly			
245	250	255			
Glu Asp Ala Pro Asp	Leu Leu Lys Val Ile Thr	Lys Pro Phe Thr Lys			
260	265	270			
Leu Ile Val Gln Leu	Asp Lys Lys Val Ile Ser	Gln Ile Ala Met Asn			
275	280	285			
Asp Glu Lys Ala Lys	Asn Lys Ser Leu Val Lys	Ile Trp Cys Lys Thr			
290	295	300			
Phe Thr Asn Lys Thr	Gln Ile Asn Val Thr Val	Pro Ser Thr Ala Asn			
305	310	315	320		
Cys Thr Ser Pro Ser	Leu Cys Trp Thr Asp	Gly Ile Gln Asn Trp Thr			
325	330	335			
Met Lys Asn Val Thr	Tyr Lys Glu Asn Ile Ala	Lys Cys Gln His Ile			
340	345	350			
Phe Val Asn Phe His	Ileu Pro Asp Leu Ala	Val Gly Thr Ile Leu Leu			
355	360	365			
Ile Leu Ser Leu Leu	Val Leu Cys Gly Cys Leu	Ile Met Ile Val Lys			
370	375	380			
Ile Leu Gly Ser Val	Leu Lys Gly Gln Val Ala	Thr Val Ile Lys Lys			
385	390	395	400		
Thr Ile Asn Thr Asp	Phe Pro Phe Pro Phe	Ala Trp Leu Thr Gly Tyr			
405	410	415			
Leu Ala Ile Leu Val	Gly Ala Gly Met Thr Phe	Ile Val Gln Ser Ser			
420	425	430			
Ser Val Phe Thr Ser	Ala Leu Thr Pro Leu Ile	Gly Ile Gly Val Ile			
435	440	445			
Thr Ile Glu Arg Ala	Tyr Pro Leu Thr Leu Gly	Ser Asn Ile Gly Thr			
450	455	460			
Thr Thr Thr Ala Ile	Leu Ala Ala Leu Ala Ser	Pro Gly Asn Ala Leu			
465	470	475	480		
Arg Ser Ser Leu Gln	Ile Ala Leu Cys His Phe	Phe Phe Asn Ile Ser			
485	490	495			
Gly Ile Leu Leu Trp	Tyr Pro Ile Pro Phe Thr	Arg Leu Pro Ile Arg			
500	505	510			
Met Ala Lys Gly Leu	Gly Asn Ile Ser Ala Lys	Tyr Arg Trp Phe Ala			
515	520	525			
Val Phe Tyr Leu Ile	Ile Phe Phe Phe Leu Ile	Pro Leu Thr Val Phe			
530	535	540			
Gly Leu Ser Leu Ala	Gly Trp Arg Val Leu Val	Gly Val Gly Val Pro			
545	550	555	560		
Val Val Phe Ile Ile	Ile Leu Val Leu Cys Leu	Arg Leu Leu Gln Ser			
565	570	575			
Arg Cys Pro Arg Val	Leu Pro Lys Lys Leu Gln	Asn Trp Asn Phe Leu			
580	585	590			
Pro Leu Trp Met Arg	Ser Leu Lys Pro Trp Asp	Ala Val Val Ser Lys			
595	600	605			
Phe Thr Gly Cys Phe	Gln Met Arg Cys Cys Cys	Cys Cys Arg Val Cys			
610	615	620			
Cys Arg Ala Cys Cys	Leu Leu Cys Gly Cys Pro	Lys Cys Cys Arg Cys			
625	630	635	640		
Ser Lys Cys Cys Glu	Asp Leu Glu Glu Ala Gln	Glu Gly Gln Asp Val			
645	650	655			
Pro Val Lys Ala Pro	Glu Thr Phe Asp Asn Ile	Thr Ile Ser Arg Glu			
660	665	670			
Ala Gln Gly Glu Val	Pro Ala Ser Asp Ser Lys	Thr Glu Cys Thr Ala			

241

675                      680                      685  
 Leu

<210> 222  
 <211> 771  
 <212> DNA  
 <213> Homo sapiens

<400> 222  
 gccgctgagc cataatggag atatcaatgc ctccacctca gatatatgta gaaaaaactc 60  
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 gatccggatt caccattgtt cagagaagaa aactacgcct cagccctgag caatgtagta 180  
 actttttatgt ggaaaagtat ggaaaaatgt ttttcccaa cttacagct tacatgagtt 240  
 ctggaccact tgtcgccatg atattagcta gacataaagc catctcttat tggttagaac 300  
 ttttgggacc aaataatagc ttagtagcga aggagacaca tccagacagt ctgagggcaa 360  
 tttatggcac agatgaccta aggaatgcac ttcatgggag taatgacttt gctgctgcgg 420  
 aaagagaaat acgttttatg tticctgaag tgattgttga gccattcca attggacaag 480  
 ctgctaagga ctatttaaat ttacatataa tgccaactct gcttgaagga ctcacagagc 540  
 tttgtaagca aaaaccagca gaccttttga tttggctagc tgattggctg ctgaaaaata 600  
 atcctaacaa acccaaactt tgtcaccatc caattgtaga agaaccttat taaaaaaaaa 660  
 atcctcgaaa gaacaaatca tgaactatct tattataaaa ggctgtactt ctactgtttg 720  
 agaaaattat ttctagggtt taagtaacta ccagtaaaat aaatttattt c 771

<210> 223  
 <211> 212  
 <212> PRT  
 <213> Homo sapiens

<400> 223  
 Met Glu Ile Ser Met Pro Pro Pro Gln Ile Tyr Val Glu Lys Thr Leu  
 1                      5                      10                      15  
 Ala Ile Ile Lys Pro Asp Ile Val Asp Lys Glu Glu Glu Ile Gln Asp  
 20                      25                      30  
 Ile Ile Leu Arg Ser Gly Phe Thr Ile Val Gln Arg Arg Lys Leu Arg  
 35                      40                      45  
 Leu Ser Pro Glu Gln Cys Ser Asn Phe Tyr Val Glu Lys Tyr Gly Lys  
 50                      55                      60  
 Met Phe Phe Pro Asn Leu Thr Ala Tyr Met Ser Ser Gly Pro Leu Val  
 65                      70                      75                      80  
 Ala Met Ile Leu Ala Arg His Lys Ala Ile Ser Tyr Trp Leu Glu Leu  
 85                      90                      95  
 Leu Gly Pro Asn Asn Ser Leu Val Ala Lys Glu Thr His Pro Asp Ser  
 100                      105                      110  
 Leu Arg Ala Ile Tyr Gly Thr Asp Asp Leu Arg Asn Ala Leu His Gly  
 115                      120                      125  
 Ser Asn Asp Phe Ala Ala Ala Glu Arg Glu Ile Arg Phe Met Phe Pro  
 130                      135                      140  
 Glu Val Ile Val Glu Pro Ile Pro Ile Gly Gln Ala Ala Lys Asp Tyr  
 145                      150                      155                      160  
 Leu Asn Leu His Ile Met Pro Thr Leu Leu Glu Gly Leu Thr Glu Leu  
 165                      170                      175  
 Cys Lys Gln Lys Pro Ala Asp Pro Leu Ile Trp Leu Ala Asp Trp Leu  
 180                      185                      190  
 Leu Lys Asn Asn Pro Asn Lys Pro Lys Leu Cys His His Pro Ile Val  
 195                      200                      205  
 Glu Glu Pro Tyr

210

<210> 224  
 <211> 3463  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 224

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actcccacgt tagggcccct gagcgacact gcccgcgcgc gggacaggtg gatgttctgg 120
gcaatgtctg cgccaccgcc accaccactt acgtcctcgc tccccgcagc cgggtcaaag 180
ccttcctctg agtcgcagcc ccccatggag gccagctctc tccccggggc tccgcccccc 240
ttcgacgccc agattcttcc cggggcgcaa ccccccttcg acgcccagtc tccccttgat 300
tctcagcctc aaccagcgg ccagccttg aatttccatg cttccacatc gtggtattgg 360
agacagtctt ctgatagggt tcctcggeat cagaagtcct tcaaccctgc agttaaaaa 420
tcttattatc cacgaaagta tgatgcaaaa ttcacagact tcagettacc tcccagtaga 480
aaacagaaaa aaaagaaaaa aaaggaacca gtttttact tttttgtga tacctgtgat 540
cgtgggttta aaatcaaga aaagtatgac aaacacatgt ctgaacatac aaaatgccct 600
gaattagatt gctcttttac tgcacacgag aagattgtcc agttccattg gagaaatatg 660
catgctcctg gcatgaagaa gatcaagtta gacactccag aggaaattgc acggtggagg 720
gaagaaagaa ggaaaaacta tccaactctg gccaatattg aaaggaagaa gaagttaaaa 780
cttgaaggagg agaagagagg agcagtattg acaacaacac aatatggcaa gatgaagggg 840
atgtccagac attcacaat ggcaagatc agaagtcctg gcaagaatca caaatggaaa 900
aacgacaatt ctagacagag agcagtcact ggatcaggca gtcacttgtg tgatttgaag 960
ctagaaggtc caccggaggc aaatgcagat cctcttggtg ttttgataaa cagtgttct 1020
gagtctgata aggaggagaa accacaacat tctgtgatac ccaaggaagt gacaccagcc 1080
ctatgccac taatgagtag ctatggcagt ctttcagggt cagagagtga gccagaagaa 1140
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ccggacattc gacatgaaag aaatgtgatt ttgcagtgtg ttcggtacat cattaaaaaa 1440
gacttttttg gactggatac taattctgcg aaaagtaaag atgtataggc atctggtgtt 1500
tcagcatata taactgaagc atgtgaaaca gtatcatcct cgttagtaga ggaaaacca 1560
aacccttttt tccgtcaaaa ttggatttgt aattaaattg taagcctcgt aggatgtatg 1620
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ttattttaat gtattgttct catgtaagaa tgactgatgt tgtgttagtt aagaattgaa 1800
gataggttta gcagtaaaga agaaagcttt taaaaggatt gattcagcta agcaaagttg 1860
ggcagagaaa tacagccatt ttgtttttaa tgcagaaaag gaagatgttc ttagcaagg 1920
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acttaattga agctttttta aaattgtaaa gtaaatgaaa gctattgaga tctttttgtc 2160
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gaacacctgg catgtgacct tagtgacgtc acagacctga gatgaagatt catgttttag 2460
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gtaacactgt tgagtgttta ctctttgtac ctctattgtg cctatattaa aggtatacaa 2640
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tgattcccaa acactcagg atgaagtaac tagtgttaca actgagttga tattctaaaa 2760
tataaccag tttgtacttt tattactagt tagcatcac attttatggc ttatgggtta 2820
ataaatgaat tcatggactc ctggactact ttcattgatg accatatctc cagggatgtt 2880
gttgatcccc aactgcctt aaggtatatt atagaaacag ttttattttc catttttctt 2940

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```

gtttcctgat aataaatgta tttaggactg aaaatactcc tgagtactcc cctggctgta 3000
tgtctgacag tctttagcta tggtagctat tgtttatttt taatgggtat ttcagattcc 3060
aagtgtattt aaaatttcta aggagatata atatagcctg tatggtttct actttatgga 3120
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gattattaaa acatttggac tattaaaaaa aaaaaaaaaa aaa 3463

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&lt;210&gt; 225

&lt;211&gt; 495

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 225

```

Met Ala Glu Pro Thr Ser Asp Phe Glu Thr Pro Ile Gly Trp His Ala
1      5      10      15
Ser Pro Glu Leu Thr Pro Thr Leu Gly Pro Leu Ser Asp Thr Ala Pro
20     25     30
Pro Arg Asp Arg Trp Met Phe Trp Ala Met Leu Pro Pro Pro Pro Pro
35     40     45
Pro Leu Thr Ser Ser Leu Pro Ala Ala Gly Ser Lys Pro Ser Ser Glu
50     55     60
Ser Gln Pro Pro Met Glu Ala Gln Ser Leu Pro Gly Ala Pro Pro Pro
65     70     75     80
Phe Asp Ala Gln Ile Leu Pro Gly Ala Gln Pro Pro Phe Asp Ala Gln
85     90     95
Ser Pro Leu Asp Ser Gln Pro Gln Pro Ser Gly Gln Pro Trp Asn Phe
100    105    110
His Ala Ser Thr Ser Trp Tyr Trp Arg Gln Ser Ser Asp Arg Phe Pro
115    120    125
Arg His Gln Lys Ser Phe Asn Pro Ala Val Lys Asn Ser Tyr Tyr Pro
130    135    140
Arg Lys Tyr Asp Ala Lys Phe Thr Asp Phe Ser Leu Pro Pro Ser Arg
145    150    155    160
Lys Gln Lys Lys Lys Lys Arg Lys Glu Pro Val Phe His Phe Phe Cys
165    170    175
Asp Thr Cys Asp Arg Gly Phe Lys Asn Gln Glu Lys Tyr Asp Lys His
180    185    190
Met Ser Glu His Thr Lys Cys Pro Glu Leu Asp Cys Ser Phe Thr Ala
195    200    205
His Glu Lys Ile Val Gln Phe His Trp Arg Asn Met His Ala Pro Gly
210    215    220
Met Lys Lys Ile Lys Leu Asp Thr Pro Glu Glu Ile Ala Arg Trp Arg
225    230    235    240
Glu Glu Arg Arg Lys Asn Tyr Pro Thr Leu Ala Asn Ile Glu Arg Lys
245    250    255
Lys Lys Leu Lys Leu Glu Lys Glu Lys Arg Gly Ala Val Leu Thr Thr
260    265    270
Thr Gln Tyr Gly Lys Met Lys Gly Met Ser Arg His Ser Gln Met Ala
275    280    285
Lys Ile Arg Ser Pro Gly Lys Asn His Lys Trp Lys Asn Asp Asn Ser
290    295    300
Arg Gln Arg Ala Val Thr Gly Ser Gly Ser His Leu Cys Asp Leu Lys
305    310    315    320
Leu Glu Gly Pro Pro Glu Ala Asn Ala Asp Pro Leu Gly Val Leu Ile
325    330    335

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244

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Asn Ser Asp Ser Glu Ser Asp Lys Glu Glu Lys Pro Gln His Ser Val
      340                      345                      350
Ile Pro Lys Glu Val Thr Pro Ala Leu Cys Ser Leu Met Ser Ser Tyr
      355                      360                      365
Gly Ser Leu Ser Gly Ser Glu Ser Glu Pro Glu Glu Thr Pro Ile Lys
      370                      375                      380
Thr Glu Ala Asp Val Leu Ala Glu Asn Gln Val Leu Asp Ser Ser Ala
      385                      390                      395                      400
Pro Lys Ser Pro Ser Gln Asp Val Lys Ala Thr Val Arg Asn Phe Ser
      405                      410                      415
Glu Ala Lys Ser Glu Asn Arg Lys Lys Ser Phe Glu Lys Thr Asn Pro
      420                      425                      430
Lys Arg Lys Lys Asp Tyr His Asn Tyr Gln Thr Leu Phe Glu Pro Arg
      435                      440                      445
Thr His His Pro Tyr Leu Leu Glu Met Leu Leu Ala Pro Asp Ile Arg
      450                      455                      460
His Glu Arg Asn Val Ile Leu Gln Cys Val Arg Tyr Ile Ile Lys Lys
      465                      470                      475                      480
Asp Phe Phe Gly Leu Asp Thr Asn Ser Ala Lys Ser Lys Asp Val
      485                      490                      495

```

<210> 226  
 <211> 942  
 <212> DNA  
 <213> Homo sapiens

```

<400> 226
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caggctgatt ctggaagttc tgaggaaaag cagctttaca acaaataccc agatgctgtg 120
gccacatggc taaaccctga cccatctcag aagcagaatc tcctagcccc acagaatgct 180
gtgtcctctg aagaaaccaa tgactttaaa caagagaccc ttccaagtaa gtccaacgaa 240
agccatgacc acatggatga tatggatgat gaagatgatg atgacatgtg ggacagccag 300
gactccattg actcgaacga ctctgatgat gtagatgaca ctgatgattc tcaccagtct 360
gatgagtctc accattctga tgaatctgat gaactggtea ctgattttcc caccggacctg 420
ccagcaaccg aagttttcac tccagttgtc cccacagtag acacatatga tggccgaggt 480
gatagtgtgg tttatggact gaggtcaaaa tctaagaagt ttgcagacc tgacatccag 540
taccctgatg ctacagacga gcacatcacc tcacacatgg aaagcgagga gttgaatggt 600
gcatacaagg ccatccccgt tgcccaggac ctgaacgcgc cttctgattg ggacagccgt 660
gggaaggaca gttatgaaac gagtcagctg gatgaccaga gtgctgaagc ccacagccac 720
aagcagtcca gattatataa gcgaaagct aatgatgaga gcaatgagca ttccgatgtg 780
attgatagtc aggaactttc caaagtcagc cgtgaattcc acagccatga atttcacagc 840
catgaagata tgctgggtgt agaccccaaa agtaaggaag aagataaaca cctgaaattt 900
cgtattttctc atgaattaga tagtgcatct tctgaggtca at 942

```

<210> 227  
 <211> 314  
 <212> PRT  
 <213> Homo sapiens

```

<400> 227
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
  1           5           10           15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
      20           25           30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
      35           40           45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Asn Ala Val Ser Ser Glu

```



245

50		55		60
Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro Ser Lys Ser Asn Glu				
65		70		75
Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp Asp His				
	85		90	
Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp				
	100		105	
Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu				
	115		120	
Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu				
	130		135	
Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly				
	145		150	
Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg				
	165		170	
Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu His Ile Thr Ser His				
	180		185	
Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala				
	195		200	
Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser				
	210		215	
Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Ala His Ser His				
	225		230	
Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu				
	245		250	
His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu				
	260		265	
Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp				
	275		280	
Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His				
	290		295	
Glu Leu Asp Ser Ala Ser Ser Glu Val Asn			300	
305		310		

&lt;210&gt; 228

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 228

```

gcagagcaca gcatcgtcgg gaccagactc gtctcaggcc agttgcagcc ttctcagcca 60
aacgccgacc aaggaaaact cactaccatg agaattgcag tgatttgctt ttgcctccta 120
ggcatcacct gtgccatacc agttaaacag gctgattctg gaagttctga ggaaaagcag 180
ctttacaaca aatacccaga tgctgtggcc acatggctaa accctgaccc atctcagaag 240
cagaatctcc tagcccacac gacccttcca agtaagtcca acgaaagcca tgaccacatg 300
gatgatatgg atgatgaaga tgatgatgac catgtggaca gccaggactc cattgactcg 360
aacgactctg atgatgtaga tgacactgat gattctcacc agtctgatga gtctcaccat 420
tctgatgaat ctgatgaact ggtcactgat tttcccacgg acctgccagc aaccgaagtt 480
ttcactccag ttgtccccac agtagacaca tatgatggcc gaggtgatag tgtggtttat 540
ggactgaggt caaaatctaa gaagtttcgc agacctgaca tccagtaccc tgatgctaca 600
gacgaggaca tcacctcaca catggaaage gaggagtga atggtgcata caaggccatc 660
cccgttgccc aggacctgaa cgcgcttctt gattgggaca gccgtgggaa ggacagttat 720
gaaacgagtc agctggatga ccagagtgtt gaaaccaca gccacaagca gtccagatta 780
tataagcgga aagccaatga tgagagcaat gagcattccg atgtgattga tagtcaggaa 840
ctttccaaag tcagccgtga attccacagc catgaatttc acagccatga agatagtctg 900
gtttagtagc ccaaaagtaa ggaagaagat aaacacctga aatttcgtat ttctcatgaa 960
ttagatagtg catcttctga ggtcaattaa aaggagaaaa aatacaattt ctacttttgc 1020

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246

```

atttagtcaa aagaaaaaat gctttatagc aaaatgaaag agaacatgaa atgcttcttt 1080
ctcagtttat tgggtgaaatg tgtatctatt tgagtctgga aataactaat gtgtttgata 1140
attagtttag tttgtggctt catggaaact ccctgtaaac taaaagcttc agggttatgt 1200
ctatgttcat tctatagaag aaatgcaaac tatcactgta ttttaataatt tgttattctc 1260
tcatgaatag aaatttatgt agaagcaaac aaaatacttt taccactta aaaagagaat 1320
ataacatttt atgtcactat aatcttttgt tttttaagtt agtgtatatt ttgttgtgat 1380
tatctttttg tgggtgtgaat aaatctttta tcttgaatgt aataagaatt tgggtggtgtc 1440
aattgcttat ttgttttccc acggttgtcc agcaattaat aaaacataac cttttttact 1500
gcctaaaaaa aaaaaaaaaa aaaa                                     1524

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&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 229

```

Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
 1      5      10      15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
 20     25     30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
 35     40     45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser
 50     55     60
Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp
 65     70     75     80
Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp
 85     90     95
Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser
100    105    110
Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala
115    120    125
Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly
130    135    140
Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe
145    150    155    160
Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr
165    170    175
Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro
180    185    190
Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys
195    200    205
Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His
210    215    220
Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser
225    230    235    240
Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser
245    250    255
Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val
260    265    270
Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile
275    280    285
Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
290    295    300

```

&lt;210&gt; 230

&lt;211&gt; 861

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 230

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atgagaattg cagtgatttg cttttgcctc ctaggcatca cctgtgccat accagttaaa 60
caggctgatt ctggaagttc tgaggaaaag cagaatgctg tgtcctctga agaaaccaat 120
gacttttaaac aagagaccct tccaagtaag tccaacgaaa gccatgacca catggatgat 180
atggatgatg aagatgatga tgaccatgtg gacagccagg actccattga ctggaacgac 240
tctgatgatg tagatgacac tgatgattct caccagtctg atgagtctca ccattctgat 300
gaatctgatg aactggtcac tgattttccc acggacctgc cagcaaccga agttttcact 360
ccagttgtcc ccacagtaga cacatatgat ggccgaggtg atagtgtggt ttatggactg 420
aggtcaaaaat ctaagaagtt tcgcagacct gacatccagt accctgatgc tacagacgag 480
cacatcacct cacacatgga aagcgaggag ttgaatggtg catacaaggc catccccgtt 540
gccaggacc tgaacgcgcc ttctgattgg gacagccgtg ggaaggacag ttatgaaacg 600
agtcagctgg atgaccagag tgctgaagcc cacagccaca agcagtcag attatataag 660
cggaaagcta atgatgagag caatgagcat tccgatgtga ttgatagtca ggaactttcc 720
aaagtcagcc gtgaattcca cagccatgaa ttccacagcc atgaagatat gctggttgta 780
gaccccaaaa gtaagggaaga agataaacac ctgaaatttc gtatttctca tgaattagat 840
agtgcattct ctgagggtcaa t                                     861

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&lt;210&gt; 231

&lt;211&gt; 287

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 231

```

Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
 1           5           10          15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Asn
          20          25          30
Ala Val Ser Ser Glu Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro
          35          40          45
Ser Lys Ser Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu
          50          55          60
Asp Asp Asp Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp
65          70          75          80
Ser Asp Asp Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser
          85          90          95
His His Ser Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp
          100         105         110
Leu Pro Ala Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr
          115         120         125
Tyr Asp Gly Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser
          130         135         140
Lys Lys Phe Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu
          145         150         155         160
His Ile Thr Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys
          165         170         175
Ala Ile Pro Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser
          180         185         190
Arg Gly Lys Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala
          195         200         205
Glu Ala His Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn
          210         215         220
Asp Glu Ser Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser
          225         230         235         240
Lys Val Ser Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp
          245         250         255

```

248

Met Leu Val Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys  
                   260                  265                  270  
 Phe Arg Ile Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn  
                   275                  280                  285

<210> 232  
 <211> 838.  
 <212> DNA  
 <213> Homo sapiens

<400> 232  
 ctgagagcca cccacagccg cagccatgct gtgcctcctg ctcaccctgg gcgtggccct 60  
 ggtctgtggt gtcccggcca tggacatccc ccagaccaag caggacctgg agctcccaaa 120  
 gttggcaggg acctggcact ccatggccat ggcgaccaac aacatctccc tcatggcgac 180  
 actgaaggcc cctctgaggg tccacatcac ctactgttg cccacccccg aggacaacct 240  
 ggagatcggt ctgcacagat gggagaacaa cagctgtggt gagaagaagg tccttggaga 300  
 gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg aggccacgct 360  
 gctcgatact gactacgaca atttcctggt tctctgccta caggacacca ccacccccat 420  
 ccagagcatg atgtgccagt acctggccag agtcctggtg gaggacgatg agatcatgca 480  
 gggattcatc agggctttca ggcccctgcc caggcaccta tggacttgc tggacttgaa 540  
 acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc ctcctggctc 600  
 acctccgcct ccaggaagac cagactccca cccttccaca cctccagagc agtgggactt 660  
 cctcctgccc tttcaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc 720  
 gccatccccct tctctgtgca cacctgcacc acggccatgg ggaggctgct ccctgggggc 780  
 agagtctctg gcagagggtta ttaataaacc cttggagcat gaaaaaaaaa aaaaaaaaaa 838

<210> 233  
 <211> 180  
 <212> PRT  
 <213> Homo sapiens

<400> 233  
 Met Leu Cys Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val  
   1                  5                  10                  15  
 Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys  
                   20                  25                  30  
 Leu Ala Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser  
                   35                  40                  45  
 Leu Met Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu  
                   50                  55                  60  
 Leu Pro Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu  
   65                  70                  75                  80  
 Asn Asn Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Glu Asn  
                   85                  90                  95  
 Pro Lys Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu  
                   100                  105                  110  
 Leu Asp Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr  
                   115                  120                  125  
 Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu  
                   130                  135                  140  
 Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro  
   145                  150                  155                  160  
 Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu  
                   165                  170                  175  
 Pro Cys Arg Phe  
                   180

<210> 234  
 <211> 851  
 <212> DNA  
 <213> Homo sapiens

<400> 234  
 ggctccagag ctccagagcca cccacagccc cagccatgct gtgcctcctg ctcaccctgg 60  
 gcgtggccct ggtctgtggt gtcccggcca tggacatccc ccagaccaag caggacctgg 120  
 agctcccaaa actgaaggcc acctggcact ccatggccat ggcgaccaac aacatctccc 180  
 tcatggcgac actgaaggcc cctctgaggg tccacatcac ctccactgtt cccacccccg 240  
 aggacaacct ggagatcggt ctgcacagat gggagaacaa cagctgtgtt gagaagaagg 300  
 tccttgagaga gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg 360  
 aggccacgct gctcgatact gactacgaca atttcctggt tctctgccta caggacacca 420  
 ccacccccat ccagagcatg atgtgccagt acctggccag agtcctggtg gaggacgatg 480  
 agatcatgca gggattcatt agggctttca ggcccctgcc caggcaccta tggtaacttg 540  
 tggacttgaa acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc 600  
 ctctgggtg acctgtaaac ccaacagctc acctccgct ccaggaagac cagactccca 660  
 cccttcaca cctccagagc agtgggactt cctcctgccc tttcaaagaa taaccacagc 720  
 tcagaagacg atgacgtggt catctgtgtc gccatcccct tcctgtgca cacctgcacc 780  
 acggccatgg ggaggctgct ccctgggggc agagtctctg gcagaggtta ttaataaacc 840  
 cttggagcat g 851

<210> 235  
 <211> 811  
 <212> DNA  
 <213> Homo sapiens

<400> 235  
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 tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120  
 aggacctgga gctcccaaag ttggcaggga cctggcactc catggccatg gcgaccaaca 180  
 acatctccct catggcgaca ctgaaggccc ctctgagggt ccacatcacc tccactgttg 240  
 ccacccccga ggacaacctg gagatcggtc tgcacagatg ggagaacaac agctgtgttg 300  
 agaagaaggt ccttgagagag aagactggga atccaaagaa gttcaagatc aactatacgg 360  
 tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420  
 aggacaccac caccacctc cagagcatga tgtgccagta cctggccaga gtccctggtg 480  
 aggacgatga gatcatgcag ggattcatca gggctttcag gccctgccc aggcacctat 540  
 ggtacttgct ggacttgaaa cagatggaag agccgtgccg tttctagctc acctccgct 600  
 ccaggaagac cagactccca cccttcaca cctccagagc agtgggactt cctcctgccc 660  
 tttcaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc gccatcccct 720  
 tcctgtgca cacctgcacc attgccatgg ggaggctgct ccctgggggc agagtctctg 780  
 gcagaggtta ttaataaacc cttggagcat g 811

<210> 236  
 <211> 850  
 <212> DNA  
 <213> Homo sapiens

<400> 236  
 catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60  
 tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120  
 aggacctgga gctcccaaag ttggcaggga cctggcactc catggccatg gcgaccaaca 180  
 acatctccct catggcgaca ctgaaggccc ctctgagggt ccacatcacc tccactgttg 240  
 ccacccccga ggacaacctg gagatcggtc tgcacagatg ggagaacaac agctgtgttg 300  
 agaagaaggt ccttgagagag aagactgrga atccaaagaa gttcaagatc aactatacgg 360  
 tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420  
 aggacaccac caccacctc cagagcatga tgtgccagta cctggccaga gtccctggtg 480

250

```

aggacgatga gatcatgcag ggattcatca gggctttcag gcccctgccc aggcacctat 540
ggtacttgct ggacttgaaa cagatggaag agccgtgccg ttcttagtga cctgtaaacc 600
caacagctca cctccgcctc caggaagacc agactccac cctccacac ctccagagca 660
gtgggacttc ctctgccct ttcaaagaat aaccacagct cagaagacga tgacgtggtc 720
atctgtgtcg ccatccctt cctgctgcac acctgcacca cggccatggg gaggtgctc 780
cctgggggca gagtctctgg cagaggttat taataaacc ttggagcatg aaaaaaaaaa 840
aaaaaaaaa                                     850

```

<210> 237  
 <211> 598  
 <212> DNA  
 <213> Homo sapiens

```

<400> 237
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aggacctgga gctcccaaag gacaccacca ccccatcca gagcatgatg tgccagtacc 180
tgccagagat cctggtggag gacgatgaga tcatgcaggg attcatcagg gctttcaggc 240
ccctgcccag gcacctatgg tacttgctgg acttgaaca gatggaagag cctgcccgtt 300
tctaggtgag ctctgcctg gtctgcctc ctgggtgacc tgtaaaccac acagctcacc 360
tccgctcca ggaagaccag actcccaccc ttccacacct ccagagcagt gggacttct 420
cctgcccttt caaagaataa ccacagctca gaagacgatg acgtggtcat ctgtgtcgcc 480
atccctctcc tgctgcacac ctgcaccacg gccatgggga ggctgctccc tgggggcaga 540
gtctctggca gaggttatta ataaaccctt ggagcatgaa aaaaaaaaaa aaaaaaaa 598

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<210> 238  
 <211> 86  
 <212> PRT  
 <213> Homo sapiens

```

<400> 238
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
 1             5             10            15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
      20            25            30
Asp Thr Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg
      35            40            45
Val Leu Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe
      50            55            60
Arg Pro Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met
      65            70            75            80
Glu Glu Pro Cys Arg Phe
                        85

```

<210> 239  
 <211> 814  
 <212> DNA  
 <213> Homo sapiens

```

<400> 239
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aggacctgga gacactgaag gcccctctga ggtccacat cacctcactg ttgccacccc 180
ccgaggacaa cctggagatc gttctgcaca gatgggagaa caacagctgt gttgagaaga 240
aggtccttgg agagaagact grgaatccaa agaagttcaa gatcaactat acggtggcga 300
acgaggccac gctgctcgat actgactacg acaatttct gtttctctgc ctacaggaca 360
ccaccacccc catccagagc atgatgtgcc agtacctggc cagagtcctg gtggaggacg 420

```

251

```

atgagatcat gcagggattc atcagggcct tcagggccct gccaggcac ctatgg tact 480
tgctggactt gaaacagatg gaagagccgt gccgtttcta ggtgagctcc tgctggctcc 540
tgctcctgg gtgacctgta aaccaacag ctcacctcg cctccaggaa gaccagactc 600
ccacccttcc acacctccag agcagtggga cttcctcctg ccctttcaaa gaataaccac 660
agctcagaag acgatgacgt ggtcatctgt gtcgccatcc ccttcctgct gcacacctgc 720
accacggcca tggggaggct gtcctctggg ggcagagtct ctggcagagg ttattaataa 780
acccttgag catgaaaaaa aaaaaaaaaa aaaa 814

```

&lt;210&gt; 240

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 240

```

Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1      5      10      15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
20     25     30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
35     40     45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
50     55     60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
65     70     75     80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
85     90     95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
100    105    110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
115    120    125
Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp
130    135    140
Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe
145    150    155

```

&lt;210&gt; 241

&lt;211&gt; 158

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

```

Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1      5      10      15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Thr Leu Lys
20     25     30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
35     40     45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
50     55     60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
65     70     75     80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
85     90     95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
100    105    110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
115    120    125

```

Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp  
 130 135 140  
 Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe  
 145 150 155

<210> 242  
 <211> 2707  
 <212> DNA  
 <213> Homo sapiens

<400> 242  
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 aagcagttag ggctgcagc cggccggcca gggcagcggc aggcgcggcc cggacctacg 120  
 ggaggaagcc ccgagccctc ggcggtgtgc gagcgactcc ccggcgatgc ctcaaacctc 180  
 catcagatct ggccatggag ggctgaacca gctgggaggg gcctttgtga atggcagacc 240  
 tctgccggaa gtgtccgcc agcgcatcgt agacctggcc caccaggggtg taaggccctg 300  
 cgacatctct cgccagctcc gcgtcagcca tggctgcgtc agcaagatcc ttggcaggta 360  
 ctacgagact ggagcatcc ggcttgaggt gatagggggc tccaagccca aggtggccac 420  
 ccccaagggtg gtggagaaga ttggggacta caaacgccag aaccctacca tgtttgcctg 480  
 ggagatccga gaccggctcc tggctgaggg cgtctgtgac aatgacactg tgcccagtg 540  
 cagctccatt aatagaatca tccggaccaa agtgcagcaa ccattcaacc tccctatgga 600  
 cagctgcgtg gccaccaagt ccctgagtc cggacacacg ctgatcccca gctcagctgt 660  
 aactcccccg gactcaccac agtcggattc cctgggctcc acctactcca tcaatgggct 720  
 cctgggcatc gctcagcctg gcagcgacaa gaggaaaatg gatgacagt atcaggatag 780  
 ctgccgacta agcattgact cacagagcag cagcagcgga ccccgaaagc accttcgcac 840  
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 cgccataaag caggaaaccc ccgaggtgtc cagttctagc tccaccctt cctctttatc 1140  
 tagctccgcc tttttggatc tgcagcaagt cggctccggg gtcccgcctt tcaatgcctt 1200  
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 tcagcctggg acaggcccca gagagtcaca caaagggaatc tttatttatt acatgaaaaa 1620  
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 gtcccaggga aagagaacca tgccatgctg aaaaagacaa aattgaagaa gaaatgtagc 1800  
 ccccgagcgg taccaccaa aggagagaag aagcaatagc cgaggaactt ggggggatgg 1860  
 cgaatggttc ctgcccgggc ccaaggggtg cacagggcac ctccatggct ccattattaa 1920  
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 tgccgaggct ctctcacca gccaccagg gagtcacct cctcagcctc ccgctgccc 2040  
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 gctgacctct tttgcctgct gctgtgaagg tatagcacca ccccggtcc tctgcagtg 2220  
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 ctgagtgaat tgtctctctt tgccctgtgg ggcttctctc cttagatgctt ctttcttttt 2640  
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 aaaaaaa 2707



<210> 243  
 <211> 450  
 <212> PRT  
 <213> Homo sapiens

<400> 243

```

Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
          20           25           30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
          35           40           45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
          50           55           60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65          70          75          80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
          85          90          95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
          100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
          115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
          165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
          180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
          195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Gly Pro Arg Lys His Leu Arg
210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
          245          250          255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
          260          265          270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
          275          280          285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Asp Pro His Ser Pro
290          295          300
Phe Ala Ile Lys Gln Glu Thr Pro Glu Val Ser Ser Ser Ser Thr
305          310          315          320
Pro Ser Ser Leu Ser Ser Ser Ala Phe Leu Asp Leu Gln Gln Val Gly
          325          330          335
Ser Gly Val Pro Pro Phe Asn Ala Phe Pro His Ala Ala Ser Val Tyr
          340          345          350
Gly Gln Phe Thr Gly Gln Ala Leu Leu Ser Gly Arg Glu Met Val Gly
          355          360          365
Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln Gly
          370          375          380
Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu Tyr
385          390          395          400
Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu Ala

```

254

	405		410		415
Trp Arg Phe	Pro Asn Ser Ser Leu	Leu Ser Ser	Pro Tyr Tyr Tyr Ser		
	420	425	430		
Ser Thr Ser	Arg Pro Ser Ala Pro	Pro Thr Thr	Ala Thr Ala Phe Asp		
	435	440	445		
His Leu					
450					

<210> 244  
 <211> 2381  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(2381)  
 <223> n = A,T,C or G

<400> 244

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ctccacctac tccatcaatg ggctcctggg catcgctcag cctggcagcg acaagaggaa 600
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cggacccccg aagcaccttc gcacggatgc cttcagccag caccacctcg agccgctcga 720
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255

2381

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<210> 245
<211> 387
<212> PRT
<213> Homo sapiens
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			20					25					30			
Arg	Ile	Val	Asp	Leu	Ala	His	Gln	Gly	Val	Arg	Pro	Cys	Asp	Ile	Ser	
		35					40					45				
Arg	Gln	Leu	Arg	Val	Ser	His	Gly	Cys	Val	Ser	Lys	Ile	Leu	Gly	Arg	
	50					55					60					
Tyr	Tyr	Glu	Thr	Gly	Ser	Ile	Arg	Pro	Gly	Val	Ile	Gly	Gly	Ser	Lys	
65					70					75					80	
Pro	Lys	Val	Ala	Thr	Pro	Lys	Val	Val	Glu	Lys	Ile	Gly	Asp	Tyr	Lys	
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Arg	Gln	Asn	Pro	Thr	Met	Phe	Ala	Trp	Glu	Ile	Arg	Asp	Arg	Leu	Leu	
			100					105					110			
Ala	Glu	Gly	Val	Cys	Asp	Asn	Asp	Thr	Val	Pro	Ser	Val	Ser	Ser	Ile	
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Asn	Arg	Ile	Ile	Arg	Thr	Lys	Val	Gln	Gln	Pro	Phe	Asn	Leu	Pro	Met	
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Asp	Ser	Cys	Val	Ala	Thr	Lys	Ser	Leu	Ser	Pro	Gly	His	Thr	Leu	Ile	
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Pro	Ser	Ser	Ala	Val	Thr	Pro	Pro	Glu	Ser	Pro	Gln	Ser	Asp	Ser	Leu	
				165					170					175		
Gly	Ser	Thr	Tyr	Ser	Ile	Asn	Gly	Leu	Leu	Gly	Ile	Ala	Gln	Pro	Gly	
			180					185					190			
Ser	Asp	Lys	Arg	Lys	Met	Asp	Asp	Ser	Asp	Gln	Asp	Ser	Cys	Arg	Leu	
		195					200					205				
Ser	Ile	Asp	Ser	Gln	Ser	Ser	Ser	Ser	Gly	Pro	Arg	Lys	His	Leu	Arg	
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Thr	Asp	Ala	Phe	Ser	Gln	His	His	Leu	Glu	Pro	Leu	Glu	Cys	Pro	Phe	
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			245						250					255		
Gly	Glu	Gln	Gly	Leu	Tyr	Pro	Leu	Pro	Leu	Leu	Asn	Ser	Thr	Leu	Asp	
			260					265					270			
Asp	Gly	Lys	Ala	Thr	Leu	Thr	Pro	Ser	Asn	Thr	Pro	Leu	Gly	Arg	Asn	
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Leu	Ser	Thr	His	Gln	Thr	Tyr	Pro	Val	Val	Ala	Gly	Arg	Glu	Met	Val	
	290					295					300					
Gly	Pro	Thr	Leu	Pro	Gly	Tyr	Pro	Pro	His	Ile	Pro	Thr	Ser	Gly	Gln	
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Gly	Ser	Tyr	Ala	Ser	Ser	Ala	Ile	Ala	Gly	Met	Val	Ala	Gly	Ser	Glu	
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385

&lt;210&gt; 246

&lt;211&gt; 387

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

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Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
          20           25           30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
          35           40           45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
          50           55           60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
          65           70           75           80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
          85           90           95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
          100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
          115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
          130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
          145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
          165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
          180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
          195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Gly Pro Arg Lys His Leu Arg
          210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
          225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
          245          250          255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
          260          265          270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
          275          280          285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Gly Arg Glu Met Val
          290          295          300
Gly Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln
          305          310          315          320
Gly Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu
          325          330          335
Tyr Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu
          340          345          350
Ala Trp Gly Phe Pro Asn Ser Ser Leu Leu Ser Ser Pro Tyr Tyr Tyr
          355          360          365
Ser Ser Thr Ser Arg Pro Ser Ala Pro Pro Thr Thr Ala Thr Ala Phe
          370          375          380
Asp His Leu

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385

<210> 247  
 <211> 2641  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(2641)  
 <223> n = A,T,C or G

<400> 247  
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 agccccgagc cctcggcggg ctgcgagcga ctccccggcg atgcctcaca actccatcag 180  
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 ggtggtggag aagattgggg actacaaacg ccagaaccct accatgtttg cctgggagat 480  
 ccgagaccgg ctctggctg agggcgtctg tgacaatgac actgtgcccga gtgtcagctc 540  
 cattaataga atcatccgga ccaaagtgcg gcaaccattc aacctcccta tggacagctg 600  
 cgtggccacc aagtccctga gtcccggaca cacgctgac cccagctcag ctgtaactcc 660  
 cccggagtca cccagctggg attccctggg ctccacctac tccatcaatg ggctcctggg 720  
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 actaagcatt gactcacaga gcagcagcag cggaccccga aagcaccttc gcacggatgc 840  
 ctccagccag caccacctcg agccgctcga gtgcccattt gagcggcagc actaccaga 900  
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 caacagcacc ctggacgacg ggaaggccac cctgaccctt tccaacacgc cactggggcg 1020  
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 tcacacaaag gaatctttat tattacatga aaaataacca caagtccagc attgcggcac 1560  
 actccctgtg tgggttaattt aatgaaccat gaaagacagg atgaccttgg acaaggccaa 1620  
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 gctgaaaaag acaaaattga agaagaaatg tagccccagc cggtagccctc caaaggagag 1740  
 aagaagcaat agccgaggaa cttgggggga tggcgaatgg ttccctgccc ggcccaaggg 1800  
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 gggagtccac tccctcagcc tcccgctgc cccacacgga ggctctggct gtcctctttc 1980  
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 cacatgactc aataaaccat tgctcttcaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 2640

a

2641

&lt;210&gt; 248

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 248

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Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
 20          25          30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
 35          40          45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
 50          55          60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
 65          70          75          80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
 85          90          95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
 100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
 115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
 130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
 145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
 165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
 180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
 195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
 210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
 225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
 245          250          255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
 260          265          270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
 275          280          285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Ala Pro Pro Phe Trp
 290          295          300
Ile Cys Ser Lys Ser Ala Pro Gly Ser Arg Pro Ser Met Pro Phe Pro
 305          310          315          320
Met Leu Pro Pro Cys Thr Gly Ser Ser Arg Ala Arg Pro Ser Ser Gln
 325          330          335
Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His Pro Thr Ser
 340          345          350
Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser Gln Ala Trp
 355          360          365
Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro Thr
 370          375          380
Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala Cys
 385          390          395

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<210> 249  
<211> 2410  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
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<223> n = A,T,C or G

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cattaataga atcatccgga ccaaagtga gcaaccattc aacctcccta tggacagctg 600  
cgtggccacc aagtcctga gtcccggaca cacgctgac cccagctcag ctgtaactcc 660  
cccggagtca cccagtcgg attccctggg ctccacctac tccatcaatg ggctcctggg 720  
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caaggccaaa ctgtcctcca agactcctta atgaggggca ggagtcccag ggaaagagaa 1440  
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aaaggagaga agaagcaata gccgaggaac ttggggggat ggcgaatggt tcctgcccgg 1560  
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ccgtcagcca ggccagcccc agggagctta aaacagacat tccacagggc ctgggcccct 1980  
gggaggtgag gtgtggtgtg cggttcacc cagggcagaa caaggcagaa tcgcaggaaa 2040  
cccgnttcc ccttctgac agtcctgcc aagccaaatg tgcttctgc agctcacgcc 2100  
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ctctgcntcc ccagcagctc ctgccccan aggcctgact gtatatactg taaatgaaac 2220  
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tctctctttg ccctgtgggg cttctctcct tgatgcttct ttcttttttt aaagacaacc 2340  
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aaaaaaaaaa 2410

<210> 250  
<211> 321  
<212> PRT

260

&lt;213&gt; Homo sapiens

&lt;400&gt; 250

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Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
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Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
          20           25           30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
          35           40           45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
          50           55           60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65           70           75           80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
          85           90           95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
          100          105          110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
          115          120          125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
          130          135          140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145          150          155          160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
          165          170          175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
          180          185          190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
          195          200          205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
          210          215          220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225          230          235          240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
          245          250          255
Gly Glu Gln Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His
          260          265          270
Pro Thr Ser Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser
          275          280          285
Gln Ala Trp Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr
          290          295          300
Pro Pro Thr Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala
305          310          315          320
Cys

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&lt;210&gt; 251

&lt;211&gt; 2308

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2308)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 251



261

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tggcctctga gtgaaatgtc tctctttgcc atgtggggt tctctccttg atgttcttt 2220
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aaaaaaaaaa aaaaaaaaaa aaaaaaaa 2308

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&lt;210&gt; 252

&lt;211&gt; 287

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

```

Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
 1             5             10             15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
          20             25             30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
          35             40             45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
          50             55             60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65             70             75             80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
          85             90             95

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262

Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu  
 100 105 110  
 Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile  
 115 120 125  
 Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met  
 130 135 140  
 Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile  
 145 150 155 160  
 Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu  
 165 170 175  
 Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly  
 180 185 190  
 Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu  
 195 200 205  
 Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg  
 210 215 220  
 Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe  
 225 230 235 240  
 Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys  
 245 250 255  
 Gly Glu Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro  
 260 265 270  
 Thr Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala Cys  
 275 280 285

&lt;210&gt; 253

&lt;211&gt; .2148

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

gcttcagggt acagctcccc cgcagccaga agccgggcct gcagcccctc agcaccgctc 60  
 cgggacaccc caccgcttc ccaggcgtga cctgtcaaca gcaacttcgc ggtgtggtga 120  
 actctctgag gaaaaacat tttgattatt actctcagac gtgcgtggca acaagtgact 180  
 gagacctaga aatccaagcg ttggaggctc tgaggccagc ctaagtcgct tcaaatgga 240  
 acgaaggcgt ttgtggggtt ccattcagag ccgatacatc agcatgagtg tgtggacaag 300  
 cccacggaga cttgtggagc tggcagggca gagcctgctg aaggatgagg ccctggccat 360  
 tgccgccttg gagttgctgc ccagggagct cttcccgcca ctcttcatgg cagcctttga 420  
 cgggagacac agccagaccc tgaaggcaat ggtgcaggcc tggcccttca cctgcctccc 480  
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 tggtttgagc acagaggcag agcagccctt cattccagta gaggtgctcg tagacctgtt 780  
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 cttgcagagt ctctgcagc acctcatcgg gctgagcaat ctgacccacg tgctgtatcc 1560

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tgttgaaaat aaagagaagc aatgtgaagc aaaaaaaaaa aaaaaaaa 2148

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&lt;210&gt; 254

&lt;211&gt; 509

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

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Met Glu Arg Arg Leu Trp Gly Ser Ile Gln Ser Arg Tyr Ile Ser
1      5      10      15
Met Ser Val Trp Thr Ser Pro Arg Arg Leu Val Glu Leu Ala Gly Gln
20     25     30
Ser Leu Leu Lys Asp Glu Ala Leu Ala Ile Ala Ala Leu Glu Leu Leu
35     40     45
Pro Arg Glu Leu Phe Pro Pro Leu Phe Met Ala Ala Phe Asp Gly Arg
50     55     60
His Ser Gln Thr Leu Lys Ala Met Val Gln Ala Trp Pro Phe Thr Cys
65     70     75     80
Leu Pro Leu Gly Val Leu Met Lys Gly Gln His Leu His Leu Glu Thr
85     90     95
Phe Lys Ala Val Leu Asp Gly Leu Asp Val Leu Leu Ala Gln Glu Val
100    105    110
Arg Pro Arg Arg Trp Lys Leu Gln Val Leu Asp Leu Arg Lys Asn Ser
115    120    125
His Gln Asp Phe Trp Thr Val Trp Ser Gly Asn Arg Ala Ser Leu Tyr
130    135    140
Ser Phe Pro Glu Pro Glu Ala Ala Gln Pro Met Thr Lys Lys Arg Lys
145    150    155    160
Val Asp Gly Leu Ser Thr Glu Ala Glu Gln Pro Phe Ile Pro Val Glu
165    170    175
Val Leu Val Asp Leu Phe Leu Lys Glu Gly Ala Cys Asp Glu Leu Phe
180    185    190
Ser Tyr Leu Ile Glu Lys Val Lys Arg Lys Lys Asn Val Leu Arg Leu
195    200    205
Cys Cys Lys Lys Leu Lys Ile Phe Ala Met Pro Met Gln Asp Ile Lys
210    215    220
Met Ile Leu Lys Met Val Gln Leu Asp Ser Ile Glu Asp Leu Glu Val
225    230    235    240
Thr Cys Thr Trp Lys Leu Pro Thr Leu Ala Lys Phe Ser Pro Tyr Leu
245    250    255
Gly Gln Met Ile Asn Leu Arg Arg Leu Leu Leu Ser His Ile His Ala
260    265    270
Ser Ser Tyr Ile Ser Pro Glu Lys Glu Glu Gln Tyr Ile Ala Gln Phe
275    280    285
Thr Ser Gln Phe Leu Ser Leu Gln Cys Leu Gln Ala Leu Tyr Val Asp
290    295    300
Ser Leu Phe Phe Leu Arg Gly Arg Leu Asp Gln Leu Leu Arg His Val
305    310    315    320
Met Asn Pro Leu Glu Thr Leu Ser Ile Thr Asn Cys Arg Leu Ser Glu

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<b>&lt;400&gt;</b>	<b>255</b>						
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ccgaccacga	gggacagcag	caccatgtcc	cacacggtcg	caggcggcgg	cagcggggac	240	
cattcccacc	aggtccgggt	gaaagcctac	taccgcgggg	atatcatgat	aacacatttt	300	
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tctcagttgg	agttagaaga	agcctttaga	ctttatgagc	taaacaagga	ttctgaactc	480	
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ctcatgtttg	agatgatggc	aggaaggtc	ccattttgata	ttgttgggag	ctccgataac	1560	
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&lt;210&gt; 256

&lt;211&gt; 587

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 256

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Met Ser His Thr Val Ala Gly Gly Gly Ser Gly Asp His Ser His Gln
 1          5          10          15
Val Arg Val Lys Ala Tyr Tyr Arg Gly Asp Ile Met Ile Thr His Phe
 20          25          30
Glu Pro Ser Ile Ser Phe Glu Gly Leu Cys Asn Glu Val Arg Asp Met
 35          40          45
Cys Ser Phe Asp Asn Glu Gln Leu Phe Thr Met Lys Trp Ile Asp Glu
 50          55          60
Glu Gly Asp Pro Cys Thr Val Ser Ser Gln Leu Glu Leu Glu Glu Ala
 65          70          75          80
Phe Arg Leu Tyr Glu Leu Asn Lys Asp Ser Glu Leu Leu Ile His Val
 85          90          95
Phe Pro Cys Val Pro Glu Arg Pro Gly Met Pro Cys Pro Gly Glu Asp
100          105          110
Lys Ser Ile Tyr Arg Arg Gly Ala Arg Arg Trp Arg Lys Leu Tyr Cys
115          120          125
Ala Asn Gly His Thr Phe Gln Ala Lys Arg Phe Asn Arg Arg Ala His
130          135          140
Cys Ala Ile Cys Thr Asp Arg Ile Trp Gly Leu Gly Arg Gln Gly Tyr
145          150          155          160
Lys Cys Ile Asn Cys Lys Leu Leu Val His Lys Lys Cys His Lys Leu
165          170          175
Val Thr Ile Glu Cys Gly Arg His Ser Leu Pro Gln Glu Pro Val Met
180          185          190
Pro Met Asp Gln Ser Ser Met His Ser Asp His Ala Gln Thr Val Ile
195          200          205
Pro Tyr Asn Pro Ser Ser His Glu Ser Leu Asp Gln Val Gly Glu Glu
210          215          220
Lys Glu Ala Met Asn Thr Arg Glu Ser Gly Lys Ala Ser Ser Ser Leu
225          230          235          240
Gly Leu Gln Asp Phe Asp Leu Leu Arg Val Ile Gly Arg Gly Ser Tyr
245          250          255
Ala Lys Val Leu Leu Val Arg Leu Lys Lys Thr Asp Arg Ile Tyr Ala
260          265          270
Met Lys Val Val Lys Lys Glu Leu Val Asn Asp Asp Glu Asp Ile Asp
275          280          285
Trp Val Gln Thr Glu Lys His Val Phe Glu Gln Ala Ser Asn His Pro
290          295          300
Phe Leu Val Gly Leu His Ser Cys Phe Gln Thr Glu Ser Arg Leu Phe
305          310          315          320

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Phe Val Ile Glu Tyr Val Asn Gly Gly Asp Leu Met Phe His Met Gln  
 325 330 335  
 Arg Gln Arg Lys Leu Pro Glu Glu His Ala Arg Phe Tyr Ser Ala Glu  
 340 345 350  
 Ile Ser Leu Ala Leu Asn Tyr Leu His Glu Arg Gly Ile Ile Tyr Arg  
 355 360 365  
 Asp Leu Lys Leu Asp Asn Val Leu Leu Asp Ser Glu Gly His Ile Lys  
 370 375 380  
 Leu Thr Asp Tyr Gly Met Cys Lys Glu Gly Leu Arg Pro Gly Asp Thr  
 385 390 395 400  
 Thr Ser Thr Phe Cys Gly Thr Pro Asn Tyr Ile Ala Pro Glu Ile Leu  
 405 410 415  
 Arg Gly Glu Asp Tyr Gly Phe Ser Val Asp Trp Trp Ala Leu Gly Val  
 420 425 430  
 Leu Met Phe Glu Met Met Ala Gly Arg Ser Pro Phe Asp Ile Val Gly  
 435 440 445  
 Ser Ser Asp Asn Pro Asp Gln Asn Thr Glu Asp Tyr Leu Phe Gln Val  
 450 455 460  
 Ile Leu Glu Lys Gln Ile Arg Ile Pro Arg Ser Leu Ser Val Lys Ala  
 465 470 475 480  
 Ala Ser Val Leu Lys Ser Phe Leu Asn Lys Asp Pro Lys Glu Arg Leu  
 485 490 495  
 Gly Cys His Pro Gln Thr Gly Phe Ala Asp Ile Gln Gly His Pro Phe  
 500 505 510  
 Phe Arg Asn Val Asp Trp Asp Met Met Glu Gln Lys Gln Val Val Pro  
 515 520 525  
 Pro Phe Lys Pro Asn Ile Ser Gly Glu Phe Gly Leu Asp Asn Phe Asp  
 530 535 540  
 Ser Gln Phe Thr Asn Glu Pro Val Gln Leu Thr Pro Asp Asp Asp Asp  
 545 550 555 560  
 Ile Val Arg Lys Ile Asp Gln Ser Glu Phe Glu Gly Phe Glu Tyr Ile  
 565 570 575  
 Asn Pro Leu Leu Met Ser Ala Glu Glu Cys Val  
 580 585

&lt;210&gt; 257

&lt;211&gt; 6742

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 257

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gtcgaccccg cgtccggcgc ggcagctctt ttctttcttc ctccacttcc cctaccctcc 60
accgtccggg agccgcgcc accgccgcg aggagtcagg aagttcaaga tggccgccgc 120
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caaggataaa aaacataaac ataagcataa acataagaaa cacaaaagaa aagagggttat 360
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tattgaaatc gttaaagaga aaacaactag gagcaagtca aaggagagga aaaaatctaa 780
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aattgaagat aaaagtaaat caaaagatag gaaaaaatcc ccaattataa atgaaagtag 960

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Lys Lys Lys His Lys His Arg Ser Lys His Lys Lys His Lys His Ser
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&lt;211&gt; 5138

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 260

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&lt;210&gt; 261

&lt;211&gt; 1834

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 261

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 <211> 343  
 <212> PRT  
 <213> Homo sapiens

<400> 262  
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<210> 263  
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 <212> DNA  
 <213> Homo sapiens

<400> 263

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&lt;210&gt; 264

&lt;211&gt; 599

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 264

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Phe Gly Leu Asp Arg Tyr Gln Cys Asp Cys Thr Arg Thr Gly Tyr Ser
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Thr	Trp	Gly	Asp	Glu	Gln	Leu	Phe	Gln	Thr	Thr	Arg	Leu	Ile	Leu	Ile	325	330	335	
Gly	Glu	Thr	Ile	Lys	Ile	Val	Ile	Glu	Glu	Tyr	Val	Gln	Gln	Leu	Ser	340	345	350	
Gly	Tyr	Phe	Leu	Gln	Leu	Lys	Phe	Asp	Pro	Glu	Leu	Leu	Phe	Gly	Val	355	360	365	
Gln	Phe	Gln	Tyr	Arg	Asn	Arg	Ile	Ala	Met	Glu	Phe	Asn	His	Leu	Tyr	370	375	380	
His	Trp	His	Pro	Leu	Met	Pro	Asp	Ser	Phe	Lys	Val	Gly	Ser	Gln	Glu	385	390	395	400
Tyr	Ser	Tyr	Glu	Gln	Phe	Leu	Phe	Asn	Thr	Ser	Met	Leu	Val	Asp	Tyr	405	410	415	
Gly	Val	Glu	Ala	Leu	Val	Asp	Ala	Phe	Ser	Arg	Gln	Ile	Ala	Gly	Arg	420	425	430	
Ile	Gly	Gly	Gly	Arg	Asn	Met	Asp	His	His	Ile	Leu	His	Val	Ala	Val	435	440	445	
Asp	Val	Ile	Arg	Glu	Ser	Arg	Glu	Met	Arg	Leu	Gln	Pro	Phe	Asn	Glu	450	455	460	
Tyr	Arg	Lys	Arg	Phe	Gly	Met	Lys	Pro	Tyr	Thr	Ser	Phe	Gln	Glu	Leu	465	470	475	480
Val	Gly	Glu	Lys	Glu	Met	Ala	Ala	Glu	Leu	Glu	Glu	Leu	Tyr	Gly	Asp	485	490	495	
Ile	Asp	Ala	Leu	Glu	Phe	Tyr	Pro	Gly	Leu	Leu	Leu	Glu	Lys	Cys	His	500	505	510	
Pro	Asn	Ser	Ile	Phe	Gly	Glu	Ser	Met	Ile	Glu	Ile	Gly	Ala	Pro	Phe	515	520	525	

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Ser Leu Lys Gly Leu Leu Gly Asn Pro Ile Cys Ser Pro Glu Tyr Trp  
 530 535 540  
 Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Asn Ile Val Lys Thr  
 545 550 555 560  
 Ala Thr Leu Lys Lys Leu Val Cys Leu Asn Thr Lys Thr Cys Pro Tyr  
 565 570 575  
 Val Ser Phe Arg Val Pro Asp Ala Ser Gln Asp Asp Gly Pro Ala Val  
 580 585 590  
 Glu Arg Pro Ser Thr Glu Leu  
 595

<210> 265  
 <211> 3000  
 <212> DNA  
 <213> Homo sapiens

<400> 265  
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 agaaatggaa agtacagact tctgaaaata tctattgaaa atgagcaact tgtgattgga 180  
 tcatatagtc agccttcaga ttcctgggat aaggattatg attcctttgt tttacccttg 240  
 ttggaggaca aacaacctag ctatatatta ttcagggttag attctcagaa tgcccaggga 300  
 tatgaatgga tattcattgc atgggtctcca gatcattctc atgttcgtca aaaaatgttg 360  
 tatgcagcaa caagagcaac tctgaagaag gaatttggag gtggccacat taaagatgaa 420  
 gtatttggaa cagtaaagga agatgtatca ttacatggat ataaaaaata cttgctgtca 480  
 caatcttccc ctgcccact gactgcagct gaggaagaac tacgacagat taaaatcaat 540  
 gaggtacaga ctgacgtggg tgtggacact aagcatcaaa cactacaagg agtagcattt 600  
 cccatttctc gagaagcctt tcaggccttg gaaaaattga ataatagaca gctcaactat 660  
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 gaactgaaag atttgccaaa gaggattccc aaggattcag ctcgttacca tttctttctg 780  
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 gaaattgtag aaagacaact acaaatggat gtaattagaa agatcgagat agacaatggg 960  
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 aattaatgtt atagaagact catgatttct atttttgagt taaagctaga aaagggttca 1320  
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<210> 266

<211> 350

<212> PRT

<213> Homo sapiens

<400> 266

Met	Ser	His	Gln	Thr	Gly	Ile	Gln	Ala	Ser	Glu	Asp	Val	Lys	Glu	Ile	1	5	10	15
Phe	Ala	Arg	Ala	Arg	Asn	Gly	Lys	Tyr	Arg	Leu	Leu	Lys	Ile	Ser	Ile	20	25	30	
Glu	Asn	Glu	Gln	Leu	Val	Ile	Gly	Ser	Tyr	Ser	Gln	Pro	Ser	Asp	Ser	35	40	45	
Trp	Asp	Lys	Asp	Tyr	Asp	Ser	Phe	Val	Leu	Pro	Leu	Leu	Glu	Asp	Lys	50	55	60	
Gln	Pro	Cys	Tyr	Ile	Leu	Phe	Arg	Leu	Asp	Ser	Gln	Asn	Ala	Gln	Gly	65	70	75	80
Tyr	Glu	Trp	Ile	Phe	Ile	Ala	Trp	Ser	Pro	Asp	His	Ser	His	Val	Arg	85	90	95	
Gln	Lys	Met	Leu	Tyr	Ala	Ala	Thr	Arg	Ala	Thr	Leu	Lys	Lys	Glu	Phe	100	105	110	
Gly	Gly	Gly	His	Ile	Lys	Asp	Glu	Val	Phe	Gly	Thr	Val	Lys	Glu	Asp	115	120	125	
Val	Ser	Leu	His	Gly	Tyr	Lys	Lys	Tyr	Leu	Leu	Ser	Gln	Ser	Ser	Pro	130	135	140	
Ala	Pro	Leu	Thr	Ala	Ala	Glu	Glu	Glu	Leu	Arg	Gln	Ile	Lys	Ile	Asn	145	150	155	160
Glu	Val	Gln	Thr	Asp	Val	Gly	Val	Asp	Thr	Lys	His	Gln	Thr	Leu	Gln	165	170	175	
Gly	Val	Ala	Phe	Pro	Ile	Ser	Arg	Glu	Ala	Phe	Gln	Ala	Leu	Glu	Lys	180	185	190	
Leu	Asn	Asn	Arg	Gln	Leu	Asn	Tyr	Val	Gln	Leu	Glu	Ile	Asp	Ile	Lys	195	200	205	
Asn	Glu	Ile	Ile	Ile	Leu	Ala	Asn	Thr	Thr	Asn	Thr	Glu	Leu	Lys	Asp	210	215	220	
Leu	Pro	Lys	Arg	Ile	Pro	Lys	Asp	Ser	Ala	Arg	Tyr	His	Phe	Phe	Leu	225	230	235	240
Tyr	Lys	His	Ser	His	Glu	Gly	Asp	Tyr	Leu	Glu	Ser	Ile	Val	Phe	Ile	245	250	255	
Tyr	Ser	Met	Pro	Gly	Tyr	Thr	Cys	Ser	Ile	Arg	Glu	Arg	Met	Leu	Tyr	260	265	270	
Ser	Ser	Cys	Lys	Ser	Arg	Leu	Leu	Glu	Ile	Val	Glu	Arg	Gln	Leu	Gln	275	280	285	
Met	Asp	Val	Ile	Arg	Lys	Ile	Glu	Ile	Asp	Asn	Gly	Asp	Glu	Leu	Thr	290	295	300	
Ala	Asp	Phe	Leu	Tyr	Glu	Glu	Val	His	Pro	Lys	Gln	His	Ala	His	Lys	305	310	315	320

280

Gln Ser Phe Ala Lys Pro Lys Gly Pro Ala Gly Lys Arg Gly Ile Arg  
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 Arg Leu Ile Arg Gly Pro Ala Glu Thr Glu Ala Thr Thr Asp  
                   340                  345                  350

<210> 267  
 <211> 358  
 <212> DNA  
 <213> Homo sapiens

<400> 267  
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 ttgcaggagg tacccggaac tccacgagt acctcgcgat ctggcccggc tcccgttcgt 180  
 cgcaacagcg tgactacagg gtatggcggg gtccgggcac tgtgcggctg gacccccagt 240  
 tctggggcca cgccgcggaa ccgcttactg ctgcagcttt tggggtcgcc cgcccgccgc 300  
 tattacagtc ttccccgcga tcagaaggtt ccattgcctt ctctttcccc cacaatgc 358

<210> 268  
 <211> 103  
 <212> PRT  
 <213> Homo sapiens

<400> 268  
 Met Trp Arg Val Cys Ala Arg Arg Ala Gln Asn Val Ala Pro Trp Ala  
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 Gly Leu Glu Ala Arg Trp Thr Ala Leu Gln Glu Val Pro Gly Thr Pro  
                   20                  25                  30  
 Arg Val Thr Ser Arg Ser Gly Pro Ala Pro Val Arg Arg Asn Ser Val  
                   35                  40                  45  
 Thr Thr Gly Tyr Gly Gly Val Arg Ala Leu Cys Gly Trp Thr Pro Ser  
                   50                  55                  60  
 Ser Gly Ala Thr Pro Arg Asn Arg Leu Leu Leu Gln Leu Leu Gly Ser  
   65                  70                  75                  80  
 Pro Gly Arg Arg Tyr Tyr Ser Leu Pro Pro His Gln Lys Val Pro Leu  
                   85                  90                  95  
 Pro Ser Leu Ser Pro Thr Met  
                   100

<210> 269  
 <211> 607  
 <212> DNA  
 <213> Homo sapiens

<400> 269  
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 ctgagctgga gacggcgatg gagaccctca tcaacgtgtt ccacgcccac tcgggcaaag 180  
 aggggggacaa gtacaagctg agcaagaagg agctgaaaga gctgtgcag acggagctct 240  
 ctggcttcct ggatgccag aaggatgtgg atgctgtgga caagtgatg aaggagctag 300  
 acgagaatgg agacggggag gtggacttcc aggagtatgt ggtgcttggt gctgctctca 360  
 cagtggcctg taacaatttc ttctgggaga acagttgagc agacagccac attgggcagc 420  
 gcccttctc tccaccctcc cagacctgcc tcttccccct gcttccacct caccacctt 480  
 atccctctcc ataaccctcc ccttgcccac cccaccccca ccccaacca gggcgcaaga 540  
 gtagcgggtcc aagcctgcaa ctcatcttcc attaaaggct tctctctcac cagcaaaaaa 600  
 aaaaaaa 607

281

<210> 270  
 <211> 94  
 <212> PRT  
 <213> Homo sapiens

<400> 270  
 Met Gly Ser Glu Leu Glu Thr Ala Met Glu Thr Leu Ile Asn Val Phe  
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 His Ala His Ser Gly Lys Glu Gly Asp Lys Tyr Lys Leu Ser Lys Lys  
 20 25 30  
 Glu Leu Lys Glu Leu Leu Gln Thr Glu Leu Ser Gly Phe Leu Asp Ala  
 35 40 45  
 Gln Lys Asp Val Asp Ala Val Asp Lys Val Met Lys Glu Leu Asp Glu  
 50 55 60  
 Asn Gly Asp Gly Glu Val Asp Phe Gln Glu Tyr Val Val Leu Val Ala  
 65 70 75 80  
 Ala Leu Thr Val Ala Cys Asn Asn Phe Phe Trp Glu Asn Ser  
 85 90

<210> 271  
 <211> 595  
 <212> DNA  
 <213> Homo sapiens

<400> 271  
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 cgcacagagc tctcagcgcc gctcccagcc acagcctccc gcgcctcgct cagctccaac 120  
 atggcaaaaa tctccagccc tacagagact gagcgggtgca tcgagtccct gattgctgtc 180  
 ttccagaagt atgctggaaa ggatggttat aactacactc tctccaagac agagttccta 240  
 agcttcatga atacagaact agctgccttc acaaagaacc agaaggaccc tgggtgcctt 300  
 gaccgcatga tgaagaaact ggacaccaac agtgatggtc agctagattt ctcagaattt 360  
 cttaatctga ttggtggcct agctatggct tgccatgact ccttcctcaa ggctgtccct 420  
 tcccagaagc ggacctgagg accccttggc cctggccttc aaaccacccc cctttccttc 480  
 cagcctttct gtcatcatct ccacagccca cccatccctt gagcacacta accacctcat 540  
 gcaggcccca cctgccaata gtaataaagc aatgtcactt ttttaaaaca tgaaa 595

<210> 272  
 <211> 105  
 <212> PRT  
 <213> Homo sapiens

<400> 272  
 Met Ala Lys Ile Ser Ser Pro Thr Glu Thr Glu Arg Cys Ile Glu Ser  
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 20 25 30  
 Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu Leu Ala  
 35 40 45  
 Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met Met  
 50 55 60  
 Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu Phe  
 65 70 75 80  
 Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe Leu  
 85 90 95  
 Lys Ala Val Pro Ser Gln Lys Arg Thr  
 100 105

<210> 273  
 <211> 428  
 <212> DNA  
 <213> Homo sapiens

<400> 273  
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 caagctgagt aagggggaaa tgaaggaact tctgcacaag gagctgcca gctttgtggg 180  
 ggagaaagtg gatgaggagg ggctgaagaa gctgatgggc agcctggatg agaacagtga 240  
 ccagcaggtg gacttccagg agtatgctgt ttctctggca ctcactactg tcatgtgcaa 300  
 tgacttcttc cagggctgcc cagaccgacc ctgaagcaga actcttgact tcctgccatg 360  
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 tctgttga 428

<210> 274  
 <211> 97  
 <212> PRT  
 <213> Homo sapiens

<400> 274  
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 20 25 30  
 Glu Met Lys Glu Leu Leu His Lys Glu Leu Pro Ser Phe Val Gly Glu  
 35 40 45  
 Lys Val Asp Glu Glu Gly Leu Lys Lys Leu Met Gly Ser Leu Asp Glu  
 50 55 60  
 Asn Ser Asp Gln Gln Val Asp Phe Gln Glu Tyr Ala Val Phe Leu Ala  
 65 70 75 80  
 Leu Ile Thr Val Met Cys Asn Asp Phe Phe Gln Gly Cys Pro Asp Arg  
 85 90 95  
 Pro

<210> 275  
 <211> 470  
 <212> DNA  
 <213> Homo sapiens

<400> 275  
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 caggccattg gcctcctcgt ggccatcttc cacaagtact ccggcaggga gggtgacaag 180  
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 aagctgcagg atgctgaaat tgcaaggctg atggaagact tggaccggaa caaggaccag 300  
 gaggtgaact tccaggagta tgtaaccttc ctgggggcct tggctttgat ctacaatgaa 360  
 gcctcaagg gctgaaaata aatagggaag atggagacac ctctgggggt cctctctgag 420  
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<210> 276  
 <211> 90  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 276

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 20 25 30  
 Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu  
 35 40 45  
 Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys  
 50 55 60  
 Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu  
 65 70 75 80  
 Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly  
 85 90

&lt;210&gt; 277

&lt;211&gt; 3151

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

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 gcagtgtgtg ggctctgcac ctttggcatg atgtactggc aattcggcct gcttttcgga 420  
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 gggccccgcc catctccagg gggtctgca ggggccagtt cctccacctg tcctctgggg 2100  
 gggccctgag agggaaggag aggtttctca caccaaggca gatgctctc tgggtgggag 2160

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&lt;210&gt; 278

&lt;211&gt; 669

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

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Pro Glu Pro Ala Ala Pro Gln Gln Pro Thr Ala Glu Glu Glu Ala Leu
35          40          45
Ile Glu Phe His Arg Ser Tyr Arg Glu Leu Phe Glu Phe Phe Cys Asn
50          55          60
Asn Thr Thr Ile His Gly Ala Ile Arg Leu Val Cys Ser Gln His Asn
65          70          75          80
Arg Met Lys Thr Ala Phe Trp Ala Val Leu Trp Leu Cys Thr Phe Gly
85          90          95
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Pro Val Ser Leu Asn Ile Asn Leu Asn Ser Asp Lys Leu Val Phe Pro
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Ala Val Thr Ile Cys Thr Leu Asn Pro Tyr Arg Tyr Pro Glu Ile Lys
130         135         140
Glu Glu Leu Glu Glu Leu Asp Arg Ile Thr Glu Gln Thr Leu Phe Asp
145         150         155         160
Leu Tyr Lys Tyr Ser Ser Phe Thr Thr Leu Val Ala Gly Ser Arg Ser
165         170         175
Arg Arg Asp Leu Arg Gly Thr Leu Pro His Pro Leu Gln Arg Leu Arg
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Val Pro Pro Pro Pro His Gly Ala Arg Arg Ala Arg Ser Val Ala Ser
195         200         205
Ser Leu Arg Asp Asn Asn Pro Gln Val Asp Trp Lys Asp Trp Lys Ile
210         215         220
Gly Phe Gln Leu Cys Asn Gln Asn Lys Ser Asp Cys Phe Tyr Gln Thr
225         230         235         240
Tyr Ser Ser Gly Val Asp Ala Val Arg Glu Trp Tyr Arg Phe His Tyr
245         250         255
Ile Asn Ile Leu Ser Arg Leu Pro Glu Thr Leu Pro Ser Leu Glu Glu
260         265         270

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285

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      340                      345                      350
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      355                      360                      365
Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr Leu
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Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser Asp
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Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val Cys
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Tyr Ile Phe Tyr Pro Arg Pro Gln Asn Val Glu Tyr Cys Asp Tyr Arg
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Val Thr Leu Leu Ser Asn Leu Gly Ser Gln Trp Ser Leu Trp Phe Gly
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Leu Val Ile Met Phe Leu Met Leu Leu Arg Arg Phe Arg Ser Arg Tyr
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&lt;210&gt; 279

&lt;211&gt; 3174

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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<400> 279

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<210> 280  
 <211> 669  
 <212> PRT  
 <213> Homo sapiens

<400> 280

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Pro	Glu	Pro	Ala	Ala	Pro	Gln	Gln	Pro	Thr	Ala	Glu	Glu	Glu	Ala	Leu
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			100					105					110		
Pro	Val	Ser	Leu	Asn	Ile	Asn	Leu	Asn	Ser	Asp	Lys	Leu	Val	Phe	Pro
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Ala	Val	Thr	Ile	Cys	Thr	Leu	Asn	Pro	Tyr	Arg	Tyr	Pro	Glu	Ile	Lys
			130				135					140			
Glu	Glu	Leu	Glu	Glu	Leu	Asp	Arg	Ile	Thr	Glu	Gln	Thr	Leu	Phe	Asp
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Leu	Tyr	Lys	Tyr	Ser	Ser	Phe	Thr	Thr	Leu	Val	Ala	Gly	Ser	Arg	Ser
				165					170					175	
Arg	Arg	Asp	Leu	Arg	Gly	Thr	Leu	Pro	His	Pro	Leu	Gln	Arg	Leu	Arg
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Val	Pro	Pro	Pro	Pro	His	Gly	Ala	Arg	Arg	Ala	Arg	Ser	Val	Ala	Ser
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Ser	Leu	Arg	Asp	Asn	Asn	Pro	Gln	Val	Asp	Trp	Lys	Asp	Trp	Lys	Ile
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Gly	Phe	Gln	Leu	Cys	Asn	Gln	Asn	Lys	Ser	Asp	Cys	Phe	Tyr	Gln	Thr
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Ile	Asn	Ile	Leu	Ser	Arg	Leu	Pro	Glu	Thr	Leu	Pro	Ser	Leu	Glu	Glu
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Cys	Asn	Gln	Ala	Asn	Tyr	Ser	His	Phe	His	His	Pro	Met	Tyr	Gly	Asn
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Cys	Tyr	Thr	Phe	Asn	Asp	Lys	Asn	Asn	Ser	Asn	Leu	Trp	Met	Ser	Ser
305				310						315				320	
Met	Pro	Gly	Ile	Asn	Asn	Gly	Leu	Ser	Leu	Met	Leu	Arg	Ala	Glu	Gln
				325					330					335	
Asn	Asp	Phe	Ile	Pro	Leu	Leu	Ser	Thr	Val	Thr	Gly	Ala	Arg	Val	Met
			340					345					350		
Val	His	Gly	Gln	Asp	Glu	Pro	Ala	Phe	Met	Asp	Asp	Gly	Gly	Phe	Asn
			355			360						365			
Leu	Arg	Pro	Gly	Val	Glu	Thr	Ser	Ile	Ser	Met	Arg	Lys	Glu	Thr	Leu
			370			375					380				
Asp	Arg	Leu	Gly	Gly	Asp	Tyr	Gly	Asp	Cys	Thr	Lys	Asn	Gly	Ser	Asp
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&lt;210&gt; 282

&lt;211&gt; 176

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

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Arg Thr Tyr Ser Gly Ala Phe Val Cys Leu Glu Ile Leu Phe Gly Gly
 35          40          45
Leu Val Trp Ile Leu Val Ala Ser Ser Asn Val Pro Leu Pro Leu Leu
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Gln Gly Trp Val Met Phe Val Ser Val Thr Ala Phe Phe Phe Ser Leu
 65          70          75          80
Leu Phe Leu Gly Met Phe Leu Ser Gly Met Val Ala Gln Ile Asp Ala
 85          90          95
Asn Trp Asn Phe Leu Asp Phe Ala Tyr His Phe Thr Val Phe Val Phe
100          105          110
Tyr Phe Gly Ala Phe Leu Leu Glu Ala Ala Ala Thr Ser Leu His Asp
115          120          125
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<400> 283

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<210> 284  
 <211> 771  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 284

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Met Gly Trp Leu Thr Arg Ile Val Cys Leu Phe Trp Gly Val Leu Leu
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Thr Ala Arg Ala Asn Tyr Gln Asn Gly Lys Asn Asn Val Pro Arg Leu
      20           25           30
Lys Leu Ser Tyr Lys Glu Met Leu Glu Ser Asn Asn Val Ile Thr Phe
      35           40           45
Asn Gly Leu Ala Asn Ser Ser Ser Tyr His Thr Phe Leu Leu Asp Glu
      50           55           60
Glu Arg Ser Arg Leu Tyr Val Gly Ala Lys Asp His Ile Phe Ser Phe
      65           70           75           80
Asp Leu Val Asn Ile Lys Asp Phe Gln Lys Ile Val Trp Pro Val Ser
      85           90           95
Tyr Thr Arg Arg Asp Glu Cys Lys Trp Ala Gly Lys Asp Ile Leu Lys
      100          105          110
Glu Cys Ala Asn Phe Ile Lys Val Leu Lys Ala Tyr Asn Gln Thr His
      115          120          125
Leu Tyr Ala Cys Gly Thr Gly Ala Phe His Pro Ile Cys Thr Tyr Ile
      130          135          140
Glu Ile Gly His His Pro Glu Asp Asn Ile Phe Lys Leu Glu Asn Ser
      145          150          155          160
His Phe Glu Asn Gly Arg Gly Lys Ser Pro Tyr Asp Pro Lys Leu Leu
      165          170          175
Thr Ala Ser Leu Leu Ile Asp Gly Glu Leu Tyr Ser Gly Thr Ala Ala
      180          185          190
Asp Phe Met Gly Arg Asp Phe Ala Ile Phe Arg Thr Leu Gly His His
      195          200          205
His Pro Ile Arg Thr Glu Gln His Asp Ser Arg Trp Leu Asn Asp Pro
      210          215          220
Lys Phe Ile Ser Ala His Leu Ile Ser Glu Ser Asp Asn Pro Glu Asp
      225          230          235          240
Asp Lys Val Tyr Phe Phe Arg Glu Asn Ala Ile Asp Gly Glu His
      245          250          255
Ser Gly Lys Ala Thr His Ala Arg Ile Gly Gln Ile Cys Lys Asn Asp
      260          265          270
Phe Gly Gly His Arg Ser Leu Val Asn Lys Trp Thr Thr Phe Leu Lys
      275          280          285
Ala Arg Leu Ile Cys Ser Val Pro Gly Pro Asn Gly Ile Asp Thr His
      290          295          300
Phe Asp Glu Leu Gln Asp Val Phe Leu Met Asn Phe Lys Asp Pro Lys
      305          310          315          320
Asn Pro Val Val Tyr Gly Val Phe Thr Thr Ser Ser Asn Ile Phe Lys
      325          330          335
Gly Ser Ala Val Cys Met Tyr Ser Met Ser Asp Val Arg Arg Val Phe
      340          345          350
Leu Gly Pro Tyr Ala His Arg Asp Gly Pro Asn Tyr Gln Trp Val Pro
      355          360          365
Tyr Gln Gly Arg Val Pro Tyr Pro Arg Pro Gly Thr Cys Pro Ser Lys
      370          375          380
Thr Phe Gly Gly Phe Asp Ser Thr Lys Asp Leu Pro Asp Asp Val Ile
      385          390          395          400
Thr Phe Ala Arg Ser His Pro Ala Met Tyr Asn Pro Val Phe Pro Met
      405          410          415
Asn Asn Arg Pro Ile Val Ile Lys Thr Asp Val Asn Tyr Gln Phe Thr
      420          425          430
Gln Ile Val Val Asp Arg Val Asp Ala Glu Asp Gly Gln Tyr Asp Val

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292

435	440	445
Met Phe Ile Gly Thr Asp Val Gly Thr Val Leu Lys Val Val Ser Ile		
450	455	460
Pro Lys Glu Thr Trp Tyr Asp Leu Glu Glu Val Leu Leu Glu Glu Met		
465	470	475
Thr Val Phe Arg Glu Pro Thr Ala Ile Ser Ala Met Glu Leu Ser Thr		
485	490	495
Lys Gln Gln Gln Leu Tyr Ile Gly Ser Thr Ala Gly Val Ala Gln Leu		
500	505	510
Pro Leu His Arg Cys Asp Ile Tyr Gly Lys Ala Cys Ala Glu Cys Cys		
515	520	525
Leu Ala Arg Asp Pro Tyr Cys Ala Trp Asp Gly Ser Ala Cys Ser Arg		
530	535	540
Tyr Phe Pro Thr Ala Lys Arg Arg Thr Arg Arg Gln Asp Ile Arg Asn		
545	550	555
Gly Asp Pro Leu Thr His Cys Ser Asp Leu His His Asp Asn His His		
565	570	575
Gly His Ser Pro Glu Glu Arg Ile Ile Tyr Gly Val Glu Asn Ser Ser		
580	585	590
Thr Phe Leu Glu Cys Ser Pro Lys Ser Gln Arg Ala Leu Val Tyr Trp		
595	600	605
Gln Phe Gln Arg Arg Asn Glu Glu Arg Lys Glu Glu Ile Arg Val Asp		
610	615	620
Asp His Ile Ile Arg Thr Asp Gln Gly Leu Leu Leu Arg Ser Leu Gln		
625	630	635
Gln Lys Asp Ser Gly Asn Tyr Leu Cys His Ala Val Glu His Gly Phe		
645	650	655
Ile Gln Thr Leu Leu Lys Val Thr Leu Glu Val Ile Asp Thr Glu His		
660	665	670
Leu Glu Glu Leu Leu His Lys Asp Asp Asp Gly Asp Gly Ser Lys Thr		
675	680	685
Lys Glu Met Ser Asn Ser Met Thr Pro Ser Gln Lys Val Trp Tyr Arg		
690	695	700
Asp Phe Met Gln Leu Ile Asn His Pro Asn Leu Asn Thr Met Asp Glu		
705	710	715
Phe Cys Glu Gln Val Trp Lys Arg Asp Arg Lys Gln Arg Arg Gln Arg		
725	730	735
Pro Gly His Thr Pro Gly Asn Ser Asn Lys Trp Lys His Leu Gln Glu		
740	745	750
Asn Lys Lys Gly Arg Asn Arg Arg Thr His Glu Phe Glu Arg Ala Pro		
755	760	765
Arg Ser Val		
770		

&lt;210&gt; 285

&lt;211&gt; 3041

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

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ggagattccg gaggtcaga tccatgaagg cttccaggaa ctctccgta cctcaacca 420

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gccagacagc cagctccagc tgaccaccgg caatggcctg ttcctcagcg agggcctgaa 480
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3041

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&lt;210&gt; 286

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 286

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Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys
1           5           10          15
Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala
20          25          30
Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
35          40          45
Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln

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294

50	55	60
Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser		
65	70	75
Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr		80
	85	90
His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro		95
	100	105
Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn		110
	115	120
Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu		125
	130	135
Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys		140
145	150	155
Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu		160
	165	170
Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys		175
	180	185
Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu		190
	195	200
Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val		205
	210	215
Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val		220
225	230	235
Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys		240
	245	250
Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala		255
	260	265
Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu		270
	275	280
Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp		285
	290	295
Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr		300
305	310	315
Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe		320
	325	330
Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys		335
	340	345
Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly		350
	355	360
Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile		365
	370	375
Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu		380
385	390	395
Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr		400
	405	410
		415

Gln Lys

&lt;210&gt; 287

&lt;211&gt; 3928

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(3928)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 287

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296

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aaaaaaaaan aaaaaaaaaa aaaaaaaaaa 3928

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&lt;210&gt; 288

&lt;211&gt; 293

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

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Met Thr Gly Leu Tyr Glu Leu Val Trp Arg Val Leu His Ala Leu Leu
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Cys Leu His Arg Thr Leu Thr Ser Trp Leu Arg Val Arg Phe Gly Thr
 20          25          30
Trp Asn Trp Ile Trp Arg Arg Cys Cys Arg Ala Ala Ser Ala Ala Val
 35          40          45
Leu Ala Pro Leu Gly Phe Thr Leu Arg Lys Pro Pro Ala Val Gly Arg
 50          55          60
Asn Arg Arg His His Arg His Pro Arg Gly Gly Ser Cys Leu Ala Ala
 65          70          75          80
Ala His His Arg Met Arg Trp Arg Ala Asp Gly Arg Ser Leu Glu Lys
 85          90          95
Leu Pro Val His Met Gly Leu Val Ile Thr Glu Val Glu Gln Glu Pro
100          105          110
Ser Phe Ser Asp Ile Ala Ser Leu Val Val Trp Cys Met Ala Val Gly
115          120          125
Ile Ser Tyr Ile Ser Val Tyr Asp His Gln Gly Ile Phe Lys Arg Asn
130          135          140
Asn Ser Arg Leu Met Asp Glu Ile Leu Lys Gln Gln Gln Glu Leu Leu
145          150          155          160
Gly Leu Asp Cys Ser Lys Tyr Ser Pro Glu Phe Ala Asn Ser Asn Asp
165          170          175
Lys Asp Asp Gln Val Leu Asn Cys His Leu Ala Val Lys Val Leu Ser
180          185          190
Pro Glu Asp Gly Lys Ala Asp Ile Val Arg Ala Ala Gln Asp Phe Cys
195          200          205
Gln Leu Val Ala Gln Lys Gln Lys Arg Pro Thr Asp Leu Asp Val Asp
210          215          220
Thr Leu Ala Ser Leu Leu Ser Ser Asn Gly Cys Pro Asp Pro Asp Leu
225          230          235          240
Val Leu Lys Phe Gly Pro Val Asp Ser Thr Leu Gly Phe Leu Pro Trp
245          250          255
His Ile Arg Leu Thr Glu Ile Val Ser Leu Pro Ser His Leu Asn Ile
260          265          270
Ser Tyr Glu Asp Phe Phe Ser Ala Leu Arg Gln Tyr Ala Ala Cys Glu
275          280          285
Gln Arg Leu Gly Lys
290

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&lt;210&gt; 289

<211> 936  
 <212> DNA  
 <213> Homo sapiens

<400> 289  
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 atgctatgaa ggctgtggaa aatagtagta cagctatttg aatcagatgc aaagatgggtg 180  
 ttgtcttttg ggtagaaaaa ttagtccttt ctaaacttta tgaagaagggt tccaacaaaa 240  
 gactttttta tggtgatcgg catgttggaa tggcagtagc aggtttgttg gcagatgctc 300  
 gttcttttagc agacatagca agagaagaag cttccaactt cagatctaac tttggctaca 360  
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 acagtgtctgt tagacctttt ggctgcagtg tgaatgacgg tgcgcaactc tacatgattg 480  
 acccatcagg tgtttcatac gggttattggg gctgtgccat cggcaaagcc aggcaagctg 540  
 caaagacgga aatagagaag cttcagatga aagaaatgac ctgccgtgat atcgttaaag 600  
 aagttgcaaa aataattttac atagtacatg acgaagttaa ggataaagct tttgaactag 660  
 aactcagctg ggttggtgaa ttaactaatg gaagacatga aattgttcca aaagatataa 720  
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<210> 290  
 <211> 248  
 <212> PRT  
 <213> Homo sapiens

<400> 290  
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 20 25 30  
 Asn Ser Ser Thr Ala Ile Gly Ile Arg Cys Lys Asp Gly Val Val Phe  
 35 40 45  
 Gly Val Glu Lys Leu Val Leu Ser Lys Leu Tyr Glu Glu Gly Ser Asn  
 50 55 60  
 Lys Arg Leu Phe Asn Val Asp Arg His Val Gly Met Ala Val Ala Gly  
 65 70 75 80  
 Leu Leu Ala Asp Ala Arg Ser Leu Ala Asp Ile Ala Arg Glu Glu Ala  
 85 90 95  
 Ser Asn Phe Arg Ser Asn Phe Gly Tyr Asn Ile Pro Leu Lys His Leu  
 100 105 110  
 Ala Asp Arg Val Ala Met Tyr Val His Ala Tyr Thr Leu Tyr Ser Ala  
 115 120 125  
 Val Arg Pro Phe Gly Cys Ser Val Asn Asp Gly Ala Gln Leu Tyr Met  
 130 135 140  
 Ile Asp Pro Ser Gly Val Ser Tyr Gly Tyr Trp Gly Cys Ala Ile Gly  
 145 150 155 160  
 Lys Ala Arg Gln Ala Ala Lys Thr Glu Ile Glu Lys Leu Gln Met Lys  
 165 170 175  
 Glu Met Thr Cys Arg Asp Ile Val Lys Glu Val Ala Lys Ile Ile Tyr  
 180 185 190  
 Ile Val His Asp Glu Val Lys Asp Lys Ala Phe Glu Leu Glu Leu Ser  
 195 200 205  
 Trp Val Gly Glu Leu Thr Asn Gly Arg His Glu Ile Val Pro Lys Asp  
 210 215 220  
 Ile Arg Glu Glu Ala Glu Lys Tyr Ala Lys Glu Ser Leu Lys Glu Glu  
 225 230 235 240

Asp Glu Ser Asp Asp Asp Asn Met  
245

<210> 291  
<211> 2782  
<212> DNA  
<213> Homo sapiens

<400> 291  
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299

&lt;210&gt; 292

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 292

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Met Asp Ser Val Ala Phe Glu Asp Val Ala Val Asn Phe Thr Leu Glu
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Glu Trp Ala Leu Leu Asp Pro Ser Gln Lys Asn Leu Tyr Arg Asp Val
 20          25          30
Met Arg Glu Thr Phe Arg Asn Leu Ala Ser Val Gly Lys Gln Trp Glu
 35          40          45
Asp Gln Asn Ile Glu Asp Pro Phe Lys Ile Pro Arg Arg Asn Ile Ser
 50          55          60
His Ile Pro Glu Arg Leu Cys Glu Ser Lys Glu Gly Gly Gln Gly Glu
 65          70          75          80
Glu Thr Phe Ser Gln Ile Pro Asp Gly Ile Leu Asn Lys Lys Thr Pro
 85          90          95
Gly Val Lys Pro Cys Glu Ser Ser Val Cys Gly Glu Val Gly Met Gly
100          105          110
Pro Ser Ser Leu Asn Arg His Ile Arg Asp His Thr Gly Arg Glu Pro
115          120          125
Asn Glu Tyr Gln Glu Tyr Gly Lys Lys Ser Tyr Thr Arg Asn Gln Cys
130          135          140
Gly Arg Ala Leu Ser Tyr His Arg Ser Phe Pro Val Arg Glu Arg Thr
145          150          155          160
His Pro Gly Gly Lys Pro Tyr Asp Cys Lys Glu Cys Gly Glu Thr Phe
165          170          175
Ile Ser Leu Val Ser Ile Arg Arg His Met Leu Thr His Arg Gly Gly
180          185          190
Val Pro Tyr Lys Cys Lys Val Cys Gly Lys Ala Phe Asp Tyr Pro Ser
195          200          205
Ile Phe Arg Ile His Glu Arg Ser His Thr Gly Glu Lys Pro Tyr Glu
210          215          220
Cys Lys Gln Cys Gly Lys Ala Phe Ser Cys Ser Ser Tyr Ile Arg Ile
225          230          235          240
His Glu Arg Thr His Thr Gly Asp Lys Pro Tyr Glu Cys Lys Gln Cys
245          250          255
Gly Lys Ala Phe Ser Cys Ser Lys Tyr Ile Arg Ile His Glu Arg Thr
260          265          270
His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Ala Phe
275          280          285
Arg Cys Ala Ser Ser Val Arg Ser His Glu Arg Thr His Thr Gly Glu
290          295          300
Lys Leu Phe Glu Cys Lys Glu Cys Gly Lys Ala Leu Thr Cys Leu Ala
305          310          315          320
Ser Val Arg Arg His Met Ile Lys His Thr Gly Asn Gly Pro Tyr Lys
325          330          335
Cys Lys Val Cys Gly Lys Ala Phe Asp Phe Pro Ser Ser Phe Arg Ile
340          345          350
His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Asp Cys Lys Gln Cys
355          360          365
Gly Lys Ala Phe Ser Cys Ser Ser Ser Phe Arg Lys His Glu Arg Ile
370          375          380
His Thr Gly Glu Lys Pro Tyr Lys Cys Thr Lys Cys Gly Lys Ala Phe
385          390          395          400
Ser Arg Ser Ser Tyr Phe Arg Ile His Glu Arg Thr His Thr Gly Glu
405          410          415

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300

Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Ala Phe Ser Arg Ser Thr  
                   420                  425                  430  
 Tyr Phe Arg Val His Glu Lys Ile His Thr Gly Glu Lys Pro Tyr Glu  
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 Asn Pro Asn Pro Asn Ala Ser Val Val Pro Val Leu Ser  
                   450                  455                  460

<210> 293  
 <211> 666  
 <212> DNA  
 <213> Homo sapiens

<400> 293  
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 gtgtcaggat ttctggtctc tggctaggtt tcctgcttat gcaatagtag ctgggagagg 180  
 ccgaaagaat tctggtgggg ccacaccac tggtgaaaga ataaatagtg aggtttggca 240  
 ttggccatca gagtcactcc tgccttcacc atgaagtcca gcggcctctt ccccttcctg 300  
 gtgctgcttg ccctgggaac tctggcacct tgggctgtgg aaggctctgg aaagtgtgag 360  
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 ggggtgtgtcc ccttctgtag gctctgatcc ctcagcttag ttctgggaga cctccctgag 480  
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 gcttctctta tgcagccatg ctgtcagccc aggtcccact ctctctctct ctctctctct 600  
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 aaaaaa 666

<210> 294  
 <211> 58  
 <212> PRT  
 <213> Homo sapiens

<400> 294  
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 Thr Leu Ala Pro Trp Ala Val Glu Gly Ser Gly Lys Cys Lys Leu Glu  
                   20                  25                  30  
 Ser Leu Trp Ser Asn Leu Gly Cys Arg Val Arg Gly Gly Val Ser Leu  
                   35                  40                  45  
 Trp Cys Gly Cys Val Pro Phe Cys Arg Leu  
                   50                  55

<210> 295  
 <211> 594  
 <212> DNA  
 <213> Homo sapiens

<400> 295  
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 tgtcctccta agaaatctgc ccagtgctt agatacaaga aacctgagtg ccagagtgc 180  
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 caatgtttga tgcttaaccc cccaatttc tgtgagatgg atggccagtg caagcgtgac 360  
 ttgaagtgtt gcatgggcat gtgtgggaaa tcctgcgttt cccctgtgaa agcttgattc 420  
 ctgccatatg gaggaggctc tggagtctgt ctctgtgtgg tccaggtoct ttccaccctg 480  
 agacttggct ccaccactga tatcctcctt tggggaaagg cttggcacac agcaggcttt 540



301

caagaagtgc cagttgatca atgaataaat aaacgagcct atttctcttt gcac 594

<210> 296

<211> 132

<212> PRT

<213> Homo sapiens

<400> 296

Met	Lys	Ser	Ser	Gly	Leu	Phe	Pro	Phe	Leu	Val	Leu	Leu	Ala	Leu	Gly
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Thr	Leu	Ala	Pro	Trp	Ala	Val	Glu	Gly	Ser	Gly	Lys	Ser	Phe	Lys	Ala
			20					25					30		
Gly	Val	Cys	Pro	Pro	Lys	Lys	Ser	Ala	Gln	Cys	Leu	Arg	Tyr	Lys	Lys
		35					40					45			
Pro	Glu	Cys	Gln	Ser	Asp	Trp	Gln	Cys	Pro	Gly	Lys	Lys	Arg	Cys	Cys
	50				55					60					
Pro	Asp	Thr	Cys	Gly	Ile	Lys	Cys	Leu	Asp	Pro	Val	Asp	Thr	Pro	Asn
65					70				75					80	
Pro	Thr	Arg	Arg	Lys	Pro	Gly	Lys	Cys	Pro	Val	Thr	Tyr	Gly	Gln	Cys
			85					90					95		
Leu	Met	Leu	Asn	Pro	Pro	Asn	Phe	Cys	Glu	Met	Asp	Gly	Gln	Cys	Lys
			100				105						110		
Arg	Asp	Leu	Lys	Cys	Cys	Met	Gly	Met	Cys	Gly	Lys	Ser	Cys	Val	Ser
		115					120					125			
Pro	Val	Lys	Ala												
			130												

<210> 297

<211> 720

<212> DNA

<213> Homo sapiens

<400> 297

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<210> 298

<211> 127

<212> PRT

<213> Homo sapiens

<400> 298

Met	Asp	Val	Phe	Lys	Lys	Gly	Phe	Ser	Ile	Ala	Lys	Glu	Gly	Val	Val
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Gly	Ala	Val	Glu	Lys	Thr	Lys	Gln	Gly	Val	Thr	Glu	Ala	Ala	Glu	Lys
			20					25					30		

Thr	Lys	Glu	Gly	Val	Met	Tyr	Val	Gly	Ala	Lys	Thr	Lys	Glu	Asn	Val
	35						40				45				
Val	Gln	Ser	Val	Thr	Ser	Val	Ala	Glu	Lys	Thr	Lys	Glu	Gln	Ala	Asn
	50					55					60				
Ala	Val	Ser	Glu	Ala	Val	Val	Ser	Ser	Val	Asn	Thr	Val	Ala	Thr	Lys
65					70					75					80
Thr	Val	Glu	Glu	Ala	Glu	Asn	Ile	Ala	Val	Thr	Ser	Gly	Val	Val	Arg
				85					90					95	
Lys	Glu	Asp	Leu	Arg	Pro	Ser	Ala	Pro	Gln	Gln	Glu	Gly	Val	Ala	Ser
			100					105					110		
Lys	Glu	Lys	Glu	Glu	Val	Ala	Glu	Glu	Ala	Gln	Ser	Gly	Gly	Asp	
	115						120					125			

&lt;210&gt; 299

&lt;211&gt; 6981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 299

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304

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&lt;210&gt; 300

&lt;211&gt; 2214

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 300

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20          25          30
Gln Arg Leu His Gly Gly Ser Ala Pro Leu Pro Gln Asp Arg Gly Phe
35          40          45
Leu Val Val Gln Gly Asp Pro Arg Glu Leu Arg Leu Trp Ala Arg Gly
50          55          60
Asp Ala Arg Gly Ala Ser Arg Ala Asp Glu Lys Pro Leu Arg Arg Lys
65          70          75          80
Arg Ser Ala Ala Leu Gln Pro Glu Pro Ile Lys Val Tyr Gly Gln Val
85          90          95
Ser Leu Asn Asp Ser His Asn Gln Met Val Val His Trp Ala Gly Glu
100          105          110
Lys Ser Asn Val Ile Val Ala Leu Ala Arg Asp Ser Leu Ala Leu Ala
115          120          125
Arg Pro Lys Ser Ser Asp Val Tyr Val Ser Tyr Asp Tyr Gly Lys Ser
130          135          140
Phe Lys Lys Ile Ser Asp Lys Leu Asn Phe Gly Leu Gly Asn Arg Ser
145          150          155          160
Glu Ala Val Ile Ala Gln Phe Tyr His Ser Pro Ala Asp Asn Lys Arg
165          170          175
Tyr Ile Phe Ala Asp Ala Tyr Ala Gln Tyr Leu Trp Ile Thr Phe Asp
180          185          190
Phe Cys Asn Thr Leu Gln Gly Phe Ser Ile Pro Phe Arg Ala Ala Asp
195          200          205
Leu Leu Leu His Ser Lys Ala Ser Asn Leu Leu Leu Gly Phe Asp Arg
210          215          220
Ser His Pro Asn Lys Gln Leu Trp Lys Ser Asp Asp Phe Gly Gln Thr
225          230          235          240

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Trp Ile Met Ile Gln Glu His Val Lys Ser Phe Ser Trp Gly Ile Asp  
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 Pro Tyr Asp Lys Pro Asn Thr Ile Tyr Ile Glu Arg His Glu Pro Ser  
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 Gly Tyr Ser Thr Val Phe Arg Ser Thr Asp Phe Phe Gln Ser Arg Glu  
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 Asn Gln Glu Val Ile Leu Glu Glu Val Arg Asp Phe Gln Leu Arg Asp  
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 Lys Tyr Met Phe Ala Thr Lys Val Val His Leu Gly Ser Glu Gln  
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 Gln Ser Ser Val Gln Leu Trp Val Ser Phe Gly Arg Lys Pro Met Arg  
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 Asp Ala Ser Glu Asp Gln Val Phe Val Cys Val Ser His Ser Asn Asn  
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 Thr Leu Val Arg Tyr Phe Ala Asn Glu Pro Phe Ala Asp Phe His Arg  
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 Val Glu Gly Leu Gln Gly Val Tyr Ile Ala Thr Leu Ile Asn Gly Ser  
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 Met Asn Glu Glu Asn Met Arg Ser Val Ile Thr Phe Asp Lys Gly Gly  
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 Thr Trp Glu Phe Leu Gln Ala Pro Ala Phe Thr Gly Tyr Gly Glu Lys  
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 Lys Glu Ser Ala Pro Gly Leu Ile Ile Ala Thr Gly Ser Val Gly Lys  
 500 505 510  
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 Arg Trp Arg Glu Ala Leu Pro Gly Pro His Tyr Tyr Thr Trp Gly Asp  
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 His Gly Gly Ile Ile Thr Ala Ile Ala Gln Gly Met Glu Thr Asn Glu  
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 Ser Glu Lys Pro Val Phe Val Tyr Gly Leu Leu Thr Glu Pro Gly Glu  
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 Lys Ser Thr Val Phe Thr Ile Phe Gly Ser Asn Lys Glu Asn Val His  
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 Cys Thr Glu Asn Asp Tyr Lys Leu Trp Ser Pro Ser Asp Glu Arg Gly  
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 His Ala Thr Cys Phe Asn Gly Glu Asp Phe Asp Arg Pro Val Val Val  
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 Ser Asn Cys Ser Cys Thr Arg Glu Asp Tyr Glu Cys Asp Phe Gly Phe  
 675 680 685  
 Lys Met Ser Glu Asp Leu Ser Leu Glu Val Cys Val Pro Asp Pro Glu  
 690 695 700

306

Phe	Ser	Gly	Lys	Ser	Tyr	Ser	Pro	Pro	Val	Pro	Cys	Pro	Val	Gly	Ser	705	710	715	720
Thr	Tyr	Arg	Arg	Thr	Arg	Gly	Tyr	Arg	Lys	Ile	Ser	Gly	Asp	Thr	Cys	725	730	735	
Ser	Gly	Gly	Asp	Val	Glu	Ala	Arg	Leu	Glu	Gly	Glu	Leu	Val	Pro	Cys	740	745	750	
Pro	Leu	Ala	Glu	Glu	Asn	Glu	Phe	Ile	Leu	Tyr	Ala	Val	Arg	Lys	Ser	755	760	765	
Ile	Tyr	Arg	Tyr	Asp	Leu	Ala	Ser	Gly	Ala	Thr	Glu	Gln	Leu	Pro	Leu	770	775	780	
Thr	Gly	Leu	Arg	Ala	Ala	Val	Ala	Leu	Asp	Phe	Asp	Tyr	Glu	His	Asn	785	790	795	800
Cys	Leu	Tyr	Trp	Ser	Asp	Leu	Ala	Leu	Asp	Val	Ile	Gln	Arg	Leu	Cys	805	810	815	
Leu	Asn	Gly	Ser	Thr	Gly	Gln	Glu	Val	Ile	Ile	Asn	Ser	Gly	Leu	Glu	820	825	830	
Thr	Val	Glu	Ala	Leu	Ala	Phe	Glu	Pro	Leu	Ser	Gln	Leu	Leu	Tyr	Trp	835	840	845	
Val	Asp	Ala	Gly	Phe	Lys	Lys	Ile	Glu	Val	Ala	Asn	Pro	Asp	Gly	Asp	850	855	860	
Phe	Arg	Leu	Thr	Ile	Val	Asn	Ser	Ser	Val	Leu	Asp	Arg	Pro	Arg	Ala	865	870	875	880
Leu	Val	Leu	Val	Pro	Gln	Glu	Gly	Val	Met	Phe	Trp	Thr	Asp	Trp	Gly	885	890	895	
Asp	Leu	Lys	Pro	Gly	Ile	Tyr	Arg	Ser	Asn	Met	Asp	Gly	Ser	Ala	Ala	900	905	910	
Tyr	His	Leu	Val	Ser	Glu	Asp	Val	Lys	Trp	Pro	Asn	Gly	Ile	Ser	Val	915	920	925	
Asp	Asp	Gln	Trp	Ile	Tyr	Trp	Thr	Asp	Ala	Tyr	Leu	Glu	Cys	Ile	Glu	930	935	940	
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Pro	His	Pro	Tyr	Ala	Ile	Ala	Val	Phe	Lys	Asn	Glu	Ile	Tyr	Trp	Asp	965	970	975	
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Ile	Phe	Tyr	Lys	Gly	Lys	Asn	Thr	Gly	Ser	Asn	Ala	Cys	Val	Pro	Arg	1010	1015	1020	
Pro	Cys	Ser	Leu	Leu	Cys	Leu	Pro	Lys	Ala	Asn	Asn	Ser	Arg	Ser	Cys	1025	1030	1035	1040
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Lys	Glu	Glu	Asn	Thr	Cys	Leu	Arg	Asn	Gln	Tyr	Arg	Cys	Ser	Asn	Gly	1075	1080	1085	
Asn	Cys	Ile	Asn	Ser	Ile	Trp	Trp	Cys	Asp	Phe	Asp	Asn	Asp	Cys	Gly	1090	1095	1100	
Asp	Met	Ser	Asp	Glu	Arg	Asn	Cys	Pro	Thr	Thr	Ile	Cys	Asp	Leu	Asp	1105	1110	1115	1120
Thr	Gln	Phe	Arg	Cys	Gln	Glu	Ser	Gly	Thr	Cys	Ile	Pro	Leu	Ser	Tyr	1125	1130	1135	
Lys	Cys	Asp	Leu	Glu	Asp	Asp	Cys	Gly	Asp	Asn	Ser	Asp	Glu	Ser	His	1140	1145	1150	
Cys	Glu	Met	His	Gln	Cys	Arg	Ser	Asp	Glu	Tyr	Asn	Cys	Ser	Ser	Gly	1155	1160	1165	

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 1970 1975 1980  
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 2005 2010 2015  
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 Phe Phe Lys Ile Ser Asn Leu Lys Met Gly His Asn Tyr Thr Phe Thr  
 2085 2090 2095



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 2115 2120 2125  
 Gln Ala Ala Arg Ser Thr Asp Val Ala Ala Val Val Val Pro Ile Leu  
 2130 2135 2140  
 Phe Leu Ile Leu Leu Ser Leu Gly Val Gly Phe Ala Ile Leu Tyr Thr  
 2145 2150 2155 2160  
 Lys His Arg Arg Leu Gln Ser Ser Phe Thr Ala Phe Ala Asn Ser His  
 2165 2170 2175  
 Tyr Ser Ser Arg Leu Gly Ser Ala Ile Phe Ser Ser Gly Asp Asp Leu  
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 gagcgctcggc acctgaacgc gagcgctcc attgcgctg cgcgttgagg ggcttcccgc 240  
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 ctggcgggc tgttcgtgat ggtgtgatc ctcttcttg gagcctccat ggtctacctg 960  
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<210> 302  
 <211> 252

310

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

```

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 1           5           10           15
Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
      20           25           30
Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg
      35           40           45
Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln
 50           55           60
Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr
65           70           75           80
Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr
      85           90           95
Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser
      100           105           110
Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn
      115           120           125
Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala
      130           135           140
Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn
145           150           155           160
Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu
      165           170           175
Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu
      180           185           190
Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val
      195           200           205
Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala
      210           215           220
Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp
225           230           235           240
Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu
      245           250

```

&lt;210&gt; 303

&lt;211&gt; 1558

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1558)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 303

```

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aggcatcgcg cgccgagaag gccggggtc cccacactga aggtccggaa aggcgacttc 180
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gcgtgcctg cgcgtctcgg ctgagctggc catggcgag ctgtgcgggc tgaggcggag 360
ccgggcgttt ctgcacctgc tgggatcgct gctcctctct ggggtcctgg cggccgacct 420
agaacgcagc atccacgaga atgccacggg tgacctggcc accagcagga atgcagcgga 480
ttcctctgtc ccaagtgtc ccagaaggca ggattctgaa gacctactca gcgatatgtt 540

```

311

```

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gggcaataag aacagctacc gctctgagga ggcttgcgtg ctccgctgct tccgccagca 720
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```

&lt;210&gt; 304

&lt;211&gt; 195

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(195)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 304

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Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
 20          25          30
Ser Ile His Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala
 35          40          45
Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp
 50          55          60
His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala
 65          70          75          80
Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val
 85          90          95
Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn
100          105          110
Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg
115          120          125
Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Xaa Leu
130          135          140
Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met
145          150          155          160
Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg
165          170          175
Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu Val Lys Asn Thr
180          185          190
Tyr Val Leu
195

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&lt;210&gt; 305

&lt;211&gt; 3079

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

```

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313

<210> 306  
 <211> 807  
 <212> PRT  
 <213> Homo sapiens

<400> 306

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			20					25				30			
Thr	Leu	Asp	Lys	Val	Pro	Lys	Ser	Glu	Gly	Tyr	Cys	Ser	Arg	Ile	Leu
		35					40					45			
Arg	Ala	Gln	Gly	Thr	Arg	Arg	Glu	Gly	Tyr	Thr	Glu	Phe	Ser	Leu	Arg
	50					55					60				
Val	Glu	Gly	Asp	Pro	Asp	Phe	Tyr	Lys	Pro	Gly	Thr	Ser	Tyr	Arg	Val
65					70					75				80	
Thr	Leu	Ser	Ala	Ala	Pro	Pro	Ser	Tyr	Phe	Arg	Gly	Phe	Thr	Leu	Ile
				85					90					95	
Ala	Leu	Arg	Glu	Asn	Arg	Glu	Gly	Asp	Lys	Glu	Glu	Asp	His	Ala	Gly
			100					105					110		
Thr	Phe	Gln	Ile	Ile	Asp	Glu	Glu	Glu	Thr	Gln	Phe	Met	Ser	Asn	Cys
		115					120					125			
Pro	Val	Ala	Val	Thr	Glu	Ser	Thr	Pro	Arg	Arg	Arg	Thr	Arg	Ile	Gln
	130					135					140				
Val	Phe	Trp	Ile	Ala	Pro	Pro	Ala	Gly	Thr	Gly	Cys	Val	Ile	Leu	Lys
145					150					155				160	
Ala	Ser	Ile	Val	Gln	Lys	Arg	Ile	Ile	Tyr	Phe	Gln	Asp	Glu	Gly	Ser
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Leu	Thr	Lys	Lys	Leu	Cys	Glu	Gln	Asp	Ser	Thr	Phe	Asp	Gly	Val	Thr
			180					185					190		
Asp	Lys	Pro	Ile	Leu	Asp	Cys	Cys	Ala	Cys	Gly	Thr	Ala	Lys	Tyr	Arg
	195					200						205			
Leu	Thr	Phe	Tyr	Gly	Asn	Trp	Ser	Glu	Lys	Thr	His	Pro	Lys	Asp	Tyr
	210				215						220				
Pro	Arg	Arg	Ala	Asn	His	Trp	Ser	Ala	Ile	Ile	Gly	Gly	Ser	His	Ser
225					230					235					240
Lys	Asn	Tyr	Val	Leu	Trp	Glu	Tyr	Gly	Gly	Tyr	Ala	Ser	Glu	Gly	Val
			245						250					255	
Lys	Gln	Val	Ala	Glu	Leu	Gly	Ser	Pro	Val	Lys	Met	Glu	Glu	Glu	Ile
			260					265					270		
Arg	Gln	Gln	Ser	Asp	Glu	Val	Leu	Thr	Val	Ile	Lys	Ala	Lys	Ala	Gln
	275						280					285			
Trp	Pro	Ala	Trp	Gln	Pro	Leu	Asn	Val	Arg	Ala	Ala	Pro	Ser	Ala	Glu
	290					295					300				
Phe	Ser	Val	Asp	Arg	Thr	Arg	His	Leu	Met	Ser	Phe	Leu	Thr	Met	Met
305					310					315					320
Gly	Pro	Ser	Pro	Asp	Trp	Asn	Val	Gly	Leu	Ser	Ala	Glu	Asp	Leu	Cys
			325						330					335	
Thr	Lys	Glu	Cys	Gly	Trp	Val	Gln	Lys	Val	Val	Gln	Asp	Leu	Ile	Pro
		340						345					350		
Trp	Asp	Ala	Gly	Thr	Asp	Ser	Gly	Val	Thr	Tyr	Glu	Ser	Pro	Asn	Lys
	355						360					365			
Pro	Thr	Ile	Pro	Gln	Glu	Lys	Ile	Arg	Pro	Leu	Thr	Ser	Leu	Asp	His
	370					375					380				
Pro	Gln	Ser	Pro	Phe	Tyr	Asp	Pro	Glu	Gly	Gly	Ser	Ile	Thr	Gln	Val
385					390					395					400
Ala	Arg	Val	Val	Ile	Glu	Arg	Ile	Ala	Arg	Lys	Gly	Glu	Gln	Cys	Asn
				405					410					415	

314

Ile Val Pro Asp Asn Val Asp Asp Ile Val Ala Asp Leu Ala Pro Glu  
 420 425 430  
 Glu Lys Asp Glu Asp Asp Thr Pro Glu Thr Cys Ile Tyr Ser Asn Trp  
 435 440 445  
 Ser Pro Trp Ser Ala Cys Ser Ser Ser Thr Cys Asp Lys Gly Lys Arg  
 450 455 460  
 Met Arg Gln Arg Met Leu Lys Ala Gln Leu Asp Leu Ser Val Pro Cys  
 465 470 475 480  
 Pro Asp Thr Gln Asp Phe Gln Pro Cys Met Gly Pro Gly Cys Ser Asp  
 485 490 495  
 Glu Asp Gly Ser Thr Cys Thr Met Ser Glu Trp Ile Thr Trp Ser Pro  
 500 505 510  
 Cys Ser Ile Ser Cys Gly Met Gly Met Arg Ser Arg Glu Arg Tyr Val  
 515 520 525  
 Lys Gln Phe Pro Glu Asp Gly Ser Val Cys Thr Leu Pro Thr Glu Glu  
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 565 570 575  
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 610 615 620  
 Asp Cys Ser Val Thr Cys Gly Lys Gly Met Arg Thr Arg Gln Arg Met  
 625 630 635 640  
 Leu Lys Ser Leu Ala Glu Leu Gly Asp Cys Asn Glu Asp Leu Glu Gln  
 645 650 655  
 Val Glu Lys Cys Met Leu Pro Glu Cys Pro Ile Asp Cys Glu Leu Thr  
 660 665 670  
 Glu Trp Ser Gln Trp Ser Glu Cys Asn Lys Ser Cys Gly Lys Gly His  
 675 680 685  
 Val Ile Arg Thr Arg Met Ile Gln Met Glu Pro Gln Phe Gly Gly Ala  
 690 695 700  
 Pro Cys Pro Glu Thr Val Gln Arg Lys Lys Cys Arg Ile Arg Lys Cys  
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 725 730 735  
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 Pro Gly Cys Arg Met Arg Pro Trp Thr Ala Trp Ser Glu Cys Thr Lys  
 755 760 765  
 Leu Cys Gly Gly Gly Ile Gln Glu Arg Tyr Met Thr Val Lys Lys Arg  
 770 775 780  
 Phe Lys Ser Ser Gln Phe Thr Ser Cys Lys Asp Lys Lys Glu Ile Arg  
 785 790 795 800  
 Ala Cys Asn Val His Pro Cys  
 805

&lt;210&gt; 307

&lt;211&gt; 5108

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 307

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 308

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<212> DNA
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&lt;210&gt; 310

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Leu Arg Glu Asn Arg Glu Gly Asp Lys Glu Glu Asp His Ala Gly Thr
           225          230          235          240

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321

Phe Gln Ile Ile Asp Glu Glu Glu Thr Gln Phe Met Ser Asn Cys Pro  
 245 250 255  
 Val Ala Val Thr Glu Ser Thr Pro Arg Arg Arg Thr Arg Ile Gln Val  
 260 265 270  
 Phe Trp Ile Ala Pro Pro Ala Gly Thr Gly Cys Val Ile Leu Lys Ala  
 275 280 285  
 Ser Ile Val Gln Lys Arg Ile Ile Tyr Phe Gln Asp Glu Gly Ser Leu  
 290 295 300  
 Thr Lys Lys Leu Cys Glu Gln Asp Ser Thr Phe Asp Gly Val Thr Asp  
 305 310 315 320  
 Lys Pro Ile Leu Asp Cys Cys Ala Cys Gly Thr Ala Lys Tyr Arg Leu  
 325 330 335  
 Thr Phe Tyr Gly Asn Trp Ser Glu Lys Thr His Pro Lys Asp Tyr Pro  
 340 345 350  
 Arg Arg Ala Asn His Trp Ser Ala Ile Ile Gly Gly Ser His Ser Lys  
 355 360 365  
 Asn Tyr Val Leu Trp Glu Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys  
 370 375 380  
 Gln Val Ala Glu Leu Gly Ser Pro Val Lys Met Glu Glu Ile Arg  
 385 390 395 400  
 Gln Gln Ser Asp Glu Val Leu Thr Val Ile Lys Ala Lys Ala Gln Trp  
 405 410 415  
 Pro Ala Trp Gln Pro Leu Asn Val Arg Ala Ala Pro Ser Ala Glu Phe  
 420 425 430  
 Ser Val Asp Arg Thr Arg His Leu Met Ser Phe Leu Thr Met Met Gly  
 435 440 445  
 Pro Ser Pro Asp Trp Asn Val Gly Leu Ser Ala Glu Asp Leu Cys Thr  
 450 455 460  
 Lys Glu Cys Gly Trp Val Gln Lys Val Val Gln Asp Leu Ile Pro Trp  
 465 470 475 480  
 Asp Ala Gly Thr Asp Ser Gly Val Thr Tyr Glu Ser Pro Asn Lys Pro  
 485 490 495  
 Thr Ile Pro Gln Glu Lys Ile Arg Pro Leu Thr Ser Leu Asp His Pro  
 500 505 510  
 Gln Ser Pro Phe Tyr Asp Pro Glu Gly Gly Ser Ile Thr Gln Val Ala  
 515 520 525  
 Arg Val Ile Glu Arg Ile Ala Arg Lys Gly Glu Gln Cys Asn Ile  
 530 535 540  
 Val Pro Asp Asn Val Asp Asp Ile Val Ala Asp Leu Ala Pro Glu Glu  
 545 550 555 560  
 Lys Asp Glu Asp Asp Thr Pro Glu Thr Cys Ile Tyr Ser Asn Trp Ser  
 565 570 575  
 Pro Trp Ser Ala Cys Ser Ser Ser Thr Cys Asp Lys Gly Lys Arg Met  
 580 585 590  
 Arg Gln Arg Met Leu Lys Ala Gln Leu Asp Leu Ser Val Pro Cys Pro  
 595 600 605  
 Asp Thr Gln Asp Phe Gln Pro Cys Met Gly Pro Gly Cys Ser Asp Glu  
 610 615 620  
 Asp Gly Ser Thr Cys Thr Met Ser Glu Trp Ile Thr Trp Ser Pro Cys  
 625 630 635 640  
 Ser Ile Ser Cys Gly Met Gly Met Arg Ser Arg Glu Arg Tyr Val Lys  
 645 650 655  
 Gln Phe Pro Glu Asp Gly Ser Val Cys Thr Leu Pro Thr Glu Glu Thr  
 660 665 670  
 Glu Lys Cys Thr Val Asn Glu Glu Cys Ser Pro Ser Ser Cys Leu Met  
 675 680 685  
 Thr Glu Trp Gly Glu Trp Asp Glu Cys Ser Ala Thr Cys Gly Met Gly  
 690 695 700

322

Met Lys Lys Arg His Arg Met Ile Lys Met Asn Pro Ala Asp Gly Ser  
 705 710 715 720  
 Met Cys Lys Ala Glu Thr Ser Gln Ala Glu Lys Cys Met Met Pro Glu  
 725 730 735  
 Cys His Thr Ile Pro Cys Leu Leu Ser Pro Trp Ser Glu Trp Ser Asp  
 740 745 750  
 Cys Ser Val Thr Cys Gly Lys Gly Met Arg Thr Arg Gln Arg Met Leu  
 755 760 765  
 Lys Ser Leu Ala Glu Leu Gly Asp Cys Asn Glu Asp Leu Glu Gln Val  
 770 775 780  
 Glu Lys Cys Met Leu Pro Glu Cys Pro Ile Asp Cys Glu Leu Thr Glu  
 785 790 795 800  
 Trp Ser Gln Trp Ser Glu Cys Asn Lys Ser Cys Gly Lys Gly His Val  
 805 810 815  
 Ile Arg Thr Arg Met Ile Gln Met Glu Pro Gln Phe Leu Gln Ser Leu  
 820 825 830  
 Leu Glu Ser  
 835

&lt;210&gt; 311

&lt;211&gt; 3112

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 311

cacgcgtccg cggacgcgtg ggctgcagcc ggagaaagag gaagagggag agagagcgcg 60  
 ccagggcgag ggcaccgccc ccggtcgggc gcgctgggcc tgcccggaaat cccgcgcgct 120  
 gcgccccgcg ccccgcgccc tgccggccat gggagccggc cgccggcagg gacgacgcct 180  
 gtgagaccgc cgagcggcct cggggacat ggggagcgat cgggcccga agggcggagg 240  
 gggcccgaag gacttcggcg cgggactcaa gtacaactcc cggcacgaga aagtgaatgg 300  
 cttggaggaa ggcgtggagt tcctgccagt caacaacgtc aagaaggtgg aaaagcatgg 360  
 cccggggcgc tgggtggtgc tggcagccgt gctgatcgcc ctctcttgg tcttgcctgg 420  
 gatcggcctc ctggtgtggc atttgcagta ccgggacgtg cgtgtccaga aggtcttcaa 480  
 tggctacatg aggatcacaa atgagaatgt tgtggatgcc tacgagaact ccaactccac 540  
 tgagtttgta agcctggcca gcaaggtgaa ggacgcgctg aagctgctgt acagcggagt 600  
 cccattcctg ggccttacc acaaggagtc ggctgtgacg gccttcagcg agggcagcgt 660  
 catcgctac tactggtctg agttcagcat ccgcagcac ctggtggagg aggccgagcg 720  
 cgtcatggcc gaggagcgc tagtcatgct gccccgcgg gcgcgctccc tgaagtcctt 780  
 tgtggtcacc tcagtgggtg ctttccccac ggaactccaa acagtacaga ggaccacga 840  
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 gcagttgtgt ggcacctacc ctccctccta caacctgacc ttccactcct cccagaacgt 1140  
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 tgggctgcgg tcattcacga gacaggctcg tgttgttggg ggcacggatg cggtatgagg 1860  
 cgagtggccc tggcaggtaa gcctgcatgc tctgggcccag ggccacatct gcggtgcttc 1920

323

```

cctcatctct cccaactggc tggctctctgc cgcacactgc tacatcgatg acagaggatt 1980
cagggtactca gacccacgc agtggacggc cttcctgggc ttgcacgacc agagccagcg 2040
cagcgcccct ggggtgcagg agcgaggct caagcgcatc atctcccacc ctttcttcaa 2100
tgacttcacc ttcgactatg acatcgcgct gctggagctg gagaaaccgg cagagtacag 2160
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ttccggggga cccctgtcca gcgtggaggc ggatgggcgg atcttccagg ccggtgtggt 2460
gagctgggga gacggctgag ctacagaggaa caagccaggc gtgtacacaa ggctccctct 2520
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cagacgggtc tgagactgaa attgttttac cagctcccag ggtggacttc agtgtgtgta 3060
tttgtgtaaa tgagtaaaac attttatttc tttttaaaaa aaaaaaaaaa aa 3112

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&lt;210&gt; 312

&lt;211&gt; 782

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 312

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Met Gly Ser Asp Arg Ala Arg Lys Gly Gly Gly Gly Pro Lys Asp Phe
 1           5           10           15
Gly Ala Gly Leu Lys Tyr Asn Ser Arg His Glu Lys Val Asn Gly Leu
 20           25           30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
 35           40           45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Val Leu Ile Gly
 50           55           60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
 65           70           75           80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
 85           90           95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
 100          105          110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
 115          120          125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
 130          135          140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
 145          150          155          160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
 165          170          175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
 180          185          190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
 195          200          205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
 210          215          220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
 225          230          235          240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu

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325

705		710		715		720
Leu Ser Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu						
		725		730		735
Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly Val Val Ser						
		740		745		750
Trp Gly Asp Gly Cys Ala Gln Arg Asn Lys Pro Gly Val Tyr Thr Arg						
		755		760		765
Leu Pro Leu Phe Arg Asp Trp Ile Lys Glu Asn Thr Gly Val						
		770		775		780

<210> 313  
 <211> 2805  
 <212> DNA  
 <213> Homo sapiens

<400> 313

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gaaatcaagg	gagggtctgg	gctgggaaag	aacgaaaagg	gagtcgcgta	tagaggagag	180
gcgacagtcg	cgagccacac	tttgcaatga	aactctttag	actttctgcc	gggagagcgg	240
cccagacgcg	ccaggtctgt	agcaggaggg	cgcgaggggc	ggtccccaga	agcctacagg	300
tgagtatcgg	ttctccctt	cccggctt	ggtccggagg	aggcgggagc	agcttccctg	360
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gcgggatgtg	tcacccaaat	accagtggg	acggtcgggt	gtggaaccag	ccgggcaggt	480
cgggtagagt	ataagagccg	gagggagcgg	ccggggcgca	gacgcctgca	gaccatccca	540
gacgccggag	cccagagcccc	gacgagtc	cgcgccctcat	ccgcccgcgt	ccgggtcccg	600
ttcctccgcc	ccaccatggc	tcggggcccc	ggcctcgcgc	cgccaccgct	gcggctgccg	660
ctgctgctgc	tggtgctggc	ggcggtgacc	ggccacacgg	ccgcgcagga	caactgcacg	720
tgtcccacca	acaagatgac	cgtgtgcagc	cccgacggcc	ccggcgcccg	ctgccagtgc	780
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gcgctcgtgg	acaacgatgg	cctctacgac	ccgactgcg	accccgagg	ccgcttcaag	960
gcgcgccagt	gcaaccagac	gtcgggtgtg	tggtgcgtga	actcgggtgg	cgtgcgccgc	1020
acggacaagg	gcgacctgag	cctacgctgc	gatgagctgg	tgcgcaccca	ccacatcctc	1080
attgacctgc	gccaccgccc	caccgcggc	gccttcaacc	actcagacct	ggacgccgag	1140
ctgaggcggc	tcttcgcgca	gcgctatcgg	ctgcaccca	agttcgtggc	ggccgtgcac	1200
tacgagcagc	ccaccatcca	gatcgagctg	cggcagaaca	cgtctcagaa	ggccgcgggt	1260
gaagtggata	tcggcgatgc	cgccactact	ttcgagagg	acatcaagg	cgagtctcta	1320
ttccagggcc	gcggcgccct	ggacttgcgc	gtgcgcggag	aaaccctgca	ggtggagcgc	1380
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gtgatcacca	accggagaaa	gtcggggaag	tacaagaagg	tgagatcaa	ggaactggg	1560
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aaaccagaag	tcggcatttg	tgaaaagtcc	ctccagattt	ctatcacttt	ggtctcta	2400
ttcccaagac	ttgtattttt	tttttatttc	aaattataac	actttttttt	cccccagaag	2460

326

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tgggtgtttc atgttgctac tctgggtgtg cccaagatat cctaactggc cagtgtaaat 2520
gctattcttt ctaaataaga ttatttgga acttccttca aactgcagga gggcgagctc 2580
tgagggcacg agaagctaaa actagctgct tttgatgaaa aagagtgcc gtctttggtc 2640
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cctttgaatc ccagccctac tcgaaataag tgggtactatt tccatttagc ctttgagcaa 2760
atcacttaac tcaaaggcgt tgtggctcta agattaaacg actttt 2805

```

&lt;210&gt; 314

&lt;211&gt; 323

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 314

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Met Ala Arg Gly Pro Gly Leu Ala Pro Pro Pro Leu Arg Leu Pro Leu
 1          5          10          15
Leu Leu Leu Val Leu Ala Ala Val Thr Gly His Thr Ala Ala Gln Asp
 20          25          30
Asn Cys Thr Cys Pro Thr Asn Lys Met Thr Val Cys Ser Pro Asp Gly
 35          40          45
Pro Gly Gly Arg Cys Gln Cys Arg Ala Leu Gly Ser Gly Met Ala Val
 50          55          60
Asp Cys Ser Thr Leu Thr Ser Lys Cys Leu Leu Leu Lys Ala Arg Met
 65          70          75          80
Ser Ala Pro Lys Asn Ala Arg Thr Leu Val Arg Pro Ser Glu His Ala
 85          90          95
Leu Val Asp Asn Asp Gly Leu Tyr Asp Pro Asp Cys Asp Pro Glu Gly
100          105          110
Arg Phe Lys Ala Arg Gln Cys Asn Gln Thr Ser Val Cys Trp Cys Val
115          120          125
Asn Ser Val Gly Val Arg Arg Thr Asp Lys Gly Asp Leu Ser Leu Arg
130          135          140
Cys Asp Glu Leu Val Arg Thr His His Ile Leu Ile Asp Leu Arg His
145          150          155          160
Arg Pro Thr Ala Gly Ala Phe Asn His Ser Asp Leu Asp Ala Glu Leu
165          170          175
Arg Arg Leu Phe Arg Glu Arg Tyr Arg Leu His Pro Lys Phe Val Ala
180          185          190
Ala Val His Tyr Glu Gln Pro Thr Ile Gln Ile Glu Leu Arg Gln Asn
195          200          205
Thr Ser Gln Lys Ala Ala Gly Glu Val Asp Ile Gly Asp Ala Ala Tyr
210          215          220
Tyr Phe Glu Arg Asp Ile Lys Gly Glu Ser Leu Phe Gln Gly Arg Gly
225          230          235          240
Gly Leu Asp Leu Arg Val Arg Gly Glu Pro Leu Gln Val Glu Arg Thr
245          250          255
Leu Ile Tyr Tyr Leu Asp Glu Ile Pro Pro Lys Phe Ser Met Lys Arg
260          265          270
Leu Thr Ala Gly Leu Ile Ala Val Ile Val Val Val Val Val Ala Leu
275          280          285
Val Ala Gly Met Ala Val Leu Val Ile Thr Asn Arg Arg Lys Ser Gly
290          295          300
Lys Tyr Lys Lys Val Glu Ile Lys Glu Leu Gly Glu Leu Arg Lys Glu
305          310          315          320
Pro Ser Leu

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&lt;210&gt; 315

327

<211> 1142  
 <212> DNA  
 <213> Homo sapiens

<400> 315  
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 gcgatgctgc tcaggagcca acaggaaata acgcggagat ctgtctcctg cccctagact 180  
 acggaccctg ccggggcccta cttctccgtt actactacga caggtacacg cagagctgcc 240  
 gccagttcct gtacggggggc tgcgagggca acgccaacaa tttctacacc tgggaggctt 300  
 gcgacgatgc ttgctggagg atagaaaaag ttcccaaagt ttgcccggctg caagtgagtg 360  
 tggacgacca gtgtgagggg tccacagaaa agtatttctt taatctaagt tccatgacat 420  
 gtgaaaaatt cttttccggg ggggtgcacc ggaaccggat tgagaacagg tttccagatg 480  
 aagctacttg tatgggcttc tgcgcaccaa agaaaattcc atcattttgc tacagtccaa 540  
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 aaatatgact cactcatttc ttggggctcg attcctgatt tcagaagagg atcataactg 1080  
 aaacaacata agacaatata atcatgtgct tttaacatat ttgagaataa aaaggactag 1140  
 cc 1142

<210> 316  
 <211> 235  
 <212> PRT  
 <213> Homo sapiens

<400> 316  
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 20 25 30  
 Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu  
 35 40 45  
 Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe  
 50 55 60  
 Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu  
 65 70 75 80  
 Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys  
 85 90 95  
 Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys  
 100 105 110  
 Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly  
 115 120 125  
 Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr  
 130 135 140  
 Cys Met Gly Phe Cys Ala Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser  
 145 150 155 160  
 Pro Lys Asp Glu Gly Leu Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe  
 165 170 175  
 Asn Pro Arg Tyr Arg Thr Cys Asp Ala Phe Thr Tyr Thr Gly Cys Gly  
 180 185 190  
 Gly Asn Asp Asn Asn Phe Val Ser Arg Glu Asp Cys Lys Arg Ala Cys  
 195 200 205

Ala Lys Ala Leu Lys Lys Lys Lys Lys Met Pro Lys Leu Arg Phe Ala  
 210 215 220  
 Ser Arg Ile Arg Lys Ile Arg Lys Lys Gln Phe  
 225 230 235

<210> 317  
 <211> 2307  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(2307)  
 <223> n = A,T,C or G

<400> 317  
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 acctgccctgc actcgggcct cctccagcca gtgctgacca gggacttctg acctgctggc 180  
 cagccaggac ctgtgtgggg aggcctcct gctgccttg ggtagacaatc tcagctccag 240  
 gctacaggga gaccgggagg atcacagagc cagcatgtta caggatcctg acagtgatca 300  
 acctctgaac agcctcgatg tcaaaccct gcgcaaacc cgtatcccca tggagacctt 360  
 cagaaagggtg gggatcccca tcatcatagc actactgagc ctggcgagta tcatcattgt 420  
 ggttgctcctc atcaaagggtga ttctggataa atactacttc ctctgcgggc agcctctcca 480  
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 ggagcactgt gtcaagagct tcccgaagg gcctgcagtg gcagtcggcc tctccaagga 600  
 ccgatccaca ctgcagggtgc tggactcggc cacagggaac tggttctctg cctgtttcga 660  
 caacttcaca gaagctctcg ctgagacagc ctgtaggcag atgggctaca gcagcaaac 720  
 cactttcaga gctgtggaga ttggccaga ccaggatctg gatgtgttg aaatcacaga 780  
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<210> 318

329

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 318

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Gly Ile Pro Ile Ile Ile Ala Leu Ser Leu Ala Ser Ile Ile Ile
   35          40          45
Val Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys
   50          55          60
Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu
 65          70          75          80
Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe
      85          90          95
Pro Glu Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr
   100          105          110
Leu Gln Val Leu Asp Ser Ala Thr Gly Asn Trp Phe Ser Ala Cys Phe
   115          120          125
Asp Asn Phe Thr Glu Ala Leu Ala Glu Thr Ala Cys Arg Gln Met Gly
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Tyr Ser Ser Lys Pro Thr Phe Arg Ala Val Glu Ile Gly Pro Asp Gln
 145          150          155          160
Asp Leu Asp Val Val Glu Ile Thr Glu Asn Ser Gln Glu Leu Arg Met
      165          170          175
Arg Asn Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His
   180          185          190
Cys Leu Ala Cys Gly Lys Ser Leu Lys Thr Pro Arg Val Val Gly Gly
   195          200          205
Glu Glu Ala Ser Val Asp Ser Trp Pro Trp Gln Val Ser Ile Gln Tyr
   210          215          220
Asp Lys Gln His Val Cys Gly Gly Ser Ile Leu Asp Pro His Trp Val
 225          230          235          240
Leu Thr Ala Ala His Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp
      245          250          255
Lys Val Arg Ala Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala
   260          265          270
Val Ala Lys Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp
   275          280          285
Asn Asp Ile Ala Leu Met Lys Leu Gln Phe Pro Leu Thr Phe Ser Gly
   290          295          300
Thr Val Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro
 305          310          315          320
Ala Thr Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn Gly
      325          330          335
Gly Lys Met Ser Asp Ile Leu Leu Gln Ala Ser Val Gln Val Ile Asp
   340          345          350
Ser Thr Arg Cys Asn Ala Asp Asp Ala Tyr Gln Gly Glu Val Thr Glu
   355          360          365
Lys Met Met Cys Ala Gly Ile Pro Glu Gly Gly Val Asp Thr Cys Gln
   370          375          380
Gly Asp Ser Gly Gly Pro Leu Met Tyr Gln Ser Asp Gln Trp His Val
 385          390          395          400
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420

425

<210> 319  
<211> 3529  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 319

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331

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&lt;210&gt; 320

&lt;211&gt; 444

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 320

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Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
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Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
20     25     30
Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
35     40     45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
50     55     60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
65     70     75     80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
85     90     95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
100    105    110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
115    120    125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
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Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
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Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
165    170    175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
180    185    190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
195    200    205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg
210    215    220
Thr Gly Phe Ser Ile Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp
225    230    235    240
Phe Leu Ser Gly Leu Ala Phe Arg Val Phe His Cys Thr Gln Tyr Val
245    250    255
Arg His Ser Ser Asp Pro Phe Tyr Thr Pro Glu Pro Asp Thr Cys His
260    265    270
Glu Leu Leu Gly His Val Pro Leu Leu Ala Glu Pro Ser Phe Ala Gln
275    280    285
Phe Ser Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Glu Glu Ala
290    295    300
Val Gln Lys Leu Ala Thr Cys Tyr Phe Phe Thr Val Glu Phe Gly Leu
305    310    315    320
Cys Lys Gln Asp Gly Gln Leu Arg Val Phe Gly Ala Gly Leu Leu Ser

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332

			325					330				335			
Ser	Ile	Ser	Glu	Leu	Lys	His	Ala	Leu	Ser	Gly	His	Ala	Lys	Val	Lys
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Pro	Phe	Asp	Pro	Lys	Ile	Thr	Cys	Lys	Gln	Glu	Cys	Leu	Ile	Thr	Thr
			355				360					365			
Phe	Gln	Asp	Val	Tyr	Phe	Val	Ser	Glu	Ser	Phe	Glu	Asp	Ala	Lys	Glu
			370				375				380				
Lys	Met	Arg	Glu	Phe	Thr	Lys	Thr	Ile	Lys	Arg	Pro	Phe	Gly	Val	Lys
			385			390				395				400	
Tyr	Asn	Pro	Tyr	Thr	Arg	Ser	Ile	Gln	Ile	Leu	Lys	Asp	Thr	Lys	Ser
			405					410					415		
Ile	Thr	Ser	Ala	Met	Asn	Glu	Leu	Gln	His	Asp	Leu	Asp	Val	Val	Ser
			420					425					430		
Asp	Ala	Leu	Ala	Lys	Val	Ser	Arg	Lys	Pro	Ser	Ile				
			435				440								

&lt;210&gt; 321

&lt;211&gt; 3505

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 321

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333

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ttaaaaaaaa aaaaaaaat aaaaaa 3505

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&lt;210&gt; 322

&lt;211&gt; 466

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 322

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Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
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Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
 20           25           30
Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
 35           40           45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
 50           55           60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
 65           70           75           80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
 85           90           95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
100           105           110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
115           120           125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
130           135           140
Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
145           150           155           160
Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
165           170           175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
180           185           190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
195           200           205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg

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334

210	215	220
Thr Gly Phe Ser Ile Arg	Pro Val Ala Gly Tyr	Leu Ser Pro Arg Asp
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Phe Leu Ser Gly Leu Ala	Phe Arg Val Phe His	Cys Thr Gln Tyr Val
245	250	255
Arg His Ser Ser Asp Pro	Phe Tyr Thr Pro Glu	Pro Asp Thr Cys His
260	265	270
Glu Leu Leu Gly His Val	Pro Leu Leu Ala Glu	Pro Ser Phe Ala Gln
275	280	285
Phe Ser Gln Glu Ile Gly	Leu Ala Ser Leu Gly	Ala Ser Glu Glu Ala
290	295	300
Val Gln Lys Leu Ala Thr	Cys Tyr Phe Phe Thr	Val Glu Phe Gly Leu
305	310	315
Cys Lys Gln Asp Gly Gln	Leu Arg Val Phe Gly	Ala Gly Leu Leu Ser
325	330	335
Ser Ile Ser Glu Leu Lys	His Ala Leu Ser Gly	His Ala Lys Val Lys
340	345	350
Pro Phe Asp Pro Lys Ile	Thr Cys Lys Gln Glu	Cys Leu Ile Thr Thr
355	360	365
Phe Gln Asp Val Tyr Phe	Val Ser Glu Ser Phe	Glu Asp Ala Lys Glu
370	375	380
Lys Met Arg Glu Phe Thr	Lys Thr Ile Lys Arg	Pro Phe Gly Val Lys
385	390	395
Tyr Asn Pro Tyr Thr Arg	Ser Ile Gln Ile Leu	Lys Asp Thr Lys Ser
405	410	415
Ile Thr Ser Ala Met Asn	Glu Leu Gln His Asp	Leu Asp Val Val Ser
420	425	430
Asp Ala Leu Ala Lys Ser	Leu Asn Glu Asp Val	Leu Gln Val Ser Val
435	440	445
Phe Ala Leu Leu Leu Phe	Leu Pro Ser Leu His	Gly Glu Cys His Pro
450	455	460
Asp Thr		
465		

&lt;210&gt; 323

&lt;211&gt; 1154

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 323

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cacgagggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt 60
tgtggagcct cagcagttcc ctctttcaga actcactgcc aagagccctg aacaggagcc 120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcacccctt 240
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ctcatcgcat ccggcgttgt ggtctttgct cttgggttcc tgggctgcta tgggtgtaag 360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct 420
gaggttgcag ctgctgtggt cgccttggtg tacaccacaa tggctgagca cttcctgacg 480
ttgctggtag tgccctgccat caagaaagat tatgggtccc aggaagactt cactcaagtg 540
tggaacacca ccatgaaagg gctcaagtgc tgtggcttca ccaactatac ggattttgag 600
gactcaccct acttcaaaga gaacagtgcc tttcccccct tctgttgcaa tgacaacgtc 660
accaacacag ccaatgaaac ctgcaccaag caaaaggctc acgacaaaaa agtagagggt 720
tgcttcaatc agcttttgta tgacatccga actaatgcag tcaccgtggg tgggtgtggc 780
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agcctctata gcactcccat cagaagagat cagctcttcc tacaaccctc ccctccatga 900
ctttcatggc tcttagagcc tctgctgtct ctgcttcacg ctggaagtat cacaatcctc 960
caccacactg aaccctcaa ggtagggccca ggtctgatta ctttcaggctc cccagtgtcc 1020

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335

agcacaaggc tgaggccaaa aaaaggacca ggggatggtt ataaaataaa tcaatgaatt 1080  
 gactgcctaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa gaaaaaaaaa 1140  
 aaaaaaaaaa aagt 1154

&lt;210&gt; 324

&lt;211&gt; 258

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 324

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met  
 130 135 140  
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp  
 145 150 155 160  
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn  
 165 170 175  
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala  
 180 185 190  
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile  
 195 200 205  
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly  
 210 215 220  
 Leu Glu Phe Phe Ser Asn Ser Ala Arg Arg Pro Pro Leu Pro Glu Ser  
 225 230 235 240  
 Leu Tyr Ser Thr Pro Ile Arg Arg Asp His Val Phe Leu Gln Pro Ser  
 245 250 255  
 Pro Pro

&lt;210&gt; 325

&lt;211&gt; 1076

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 325

atgcagtgtc tcagcttcat taagaccatg atgacccctc tcaatttgct catctttctg 60  
 tgtggtgcag ccctgttggt agtgggcatc tgggtgtcaa tcgatggggc atcctttctg 120  
 aagatcttcg ggccactgtc gtcagtgcc atgcagtttg tcaacgtggg ctacttcctc 180  
 atcgagccg gcgttggtgt ctttgctcct ggtttcctgg gctgctatgg tgctaagact 240  
 gagagcaagt gtgcctcgt gacgttcttc ttcacccctc tcctcatctt cattgctgag 300  
 gttgcagctg ctgtggtcgc cttggtgtac accacaatgg ctgagcactt cctgacgttg 360

336

```

ctggtagtgc ctgccatcaa gaaagattat ggttcccagg aagacttcac tcaagtgtgg 420
aacaccacca tgaaagggct caagtgtgtt ggcttcacca actatacggg ttttgaggac 480
tcaccctact tcaaagagaa cagtgccttt cccccattct gttgcaatga caacgtcacc 540
aacacagcca atgaaacctg caccgagcaa aaggctcacg accaaaaagt agagggttgc 600
ttcaatcagc ttttgtatga catccgaact aatgcagtca ccgtgggtgg tgtggcagct 660
ggaattgggg gcctcgagct ggctgccatg attgtgtcca tgtatctgta ctgcaatcta 720
caataagtcc acttctgcct ctgccactac tgctgccaca tgggaactgt gaagaggcac 780
cctggcaagc agcagtgtat gggggagggg acaggatcta acaatgtcac ttgggccaga 840
atggacctgc cctttctgct ccagacttgg ggctagatag ggaccactcc ttttaggcga 900
tgctgacttt ccttccattg gtgggtggat ggggtggggg cattccagag cctctaaggt 960
agccagttct gttgccatt cccccagctc attaaaccct tgatatgcc cctaggccta 1020
gtggtgatcc cagtgtctta ctgggggatg agagaaaggc attttatagc ctgggc 1076

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&lt;210&gt; 326

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 326

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Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1          5          10          15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20          25          30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35          40          45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50          55          60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65          70          75          80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
 85          90          95
Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
100          105          110
Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
115          120          125
Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
130          135          140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
145          150          155          160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
165          170          175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Glu Gln Lys Ala
180          185          190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
195          200          205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
210          215          220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
225          230          235          240
Gln

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&lt;210&gt; 327

&lt;211&gt; 2244

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 327

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gggaaggaga tgcctcttcc ttcccttcaa tagtgggtta aaccagctg gcaccctctg 60
gaactacggg aacaatattc ttcaagagaa ggctactcta ccaaagccag gagcacagta 120
ttctcaggat ctcaacaagg aagagcagac caagggttget tctgattcct tacaaccttc 180
cgtaattcca ggcttgtggc cccaaattca gggccccacc cttccaggaa caaatcatta 240
tagtaataat ttgccttcat cttccatata ccaactaagc atgtttaact acgaacgtcc 300
aaaacacttc atccagtcct aaaacccatg tggctccaga ttgcagcctc ctggaccaga 360
aacctccagc ttctctagcc agaccaaaaca gtcttccatt atcatccagc cccgccagtg 420
tacagagcaa agattttctg cctcctcaac actgagctct cacatcacca tgtcctcctc 480
tgctttccct gcttctcccc agcagcatgc tggctccaac ccaggccaaa gggttacaac 540
cacctataac cagtcctccag ccagcttcct cagctccata ttaccatcac agcctgatta 600
caatagcagt aaaatccctt ccgctatgga ttccaactat caacagtcct cagctggcca 660
acctataaat gcaaagccat cccaaactgc aaatgctaag ccataccaa gaactcctga 720
tcatgaaata caaggatcaa aagaagcttt gattcaagat ttggaaagaa agctgaaatg 780
caaggacacc cttcttcata atggaaatca acgtctaaca tatgaagaga agatggctcg 840
cagattgcta ggaccacaga atgcagctgc tgtgtttcaa gctcaggatg acagtgggtc 900
acaagactcg cagcaacaca actcagaaca tgcgcgactg caagttccta catcacaagt 960
aagaagtaga tcaacctcaa ggggagatgt gaatgatcag gatgcaatcc aggagaaatt 1020
ttaccaccca cgtttcattc aagtgccaga gaacatgtcg attgatgaag gaagattctg 1080
cagaatggac ttcaaagtga gtggactgcc agctcctgat gtgtcatggt atctaaatgg 1140
aagaacagtt caatcagatg atttgcacaa aatgatagtg tctgagaagg gtcttcattc 1200
actcatcttt gaagtagtca gagcttcaga tgcaggggct tatgcatgtg ttgccaaagaa 1260
tagagcagga gaagccacct tcaactgtgca gctggatgtc cttgcaaaag aacataaaag 1320
agcaccaatg tttatctaca aaccacagag caaaaaagtt ttagaggagg attcagtga 1380
actagaatgc cagatctcgg ctatacctcc accaaagctt ttctggaaaa gaaataatga 1440
aatggtacaa ttcaacactg accgaataag cttatatcaa gataacactg gaagagtac 1500
tttactgata aaagatgtaa acaagaaaga tgcgtgggtg tatactgtgt cagcagttaa 1560
tgaagctgga gtgactacat gtaacacaag attagacgtt acygcacgtc caaaccaaac 1620
tcttccagct cctaagcagt tacgggttcg accaacattc agcaaattat tagcacttaa 1680
tgggaaagggt ttgaatgtaa aacaagcttt taaccagaa ggagaatttc agcgtttggc 1740
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agccaactac accattagta atatatgtga ttacattttt ttgaaattaa tccatagctg 1860
tattaacaga ttatggtttt aattaggtaa tatagttaat atatatatat aatattattt 1920
atcctttgac tcttgacat tctatgtacc cctccgattt gtgaagccta caggaaatct 1980
gggtatatgg atttgtaact gcagaagact atcttaaaat acaggatttt aacatttaag 2040
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gcttgtaata acggtttactg gtactgcttt cttaaatactg ttttaccctg tttctctgt 2160
aggaatacta acatggtata gattatctga gtgttcacac gttgtatgtc aaaagaaaat 2220
aaaattcaaa tatttaaaac ggac 2244

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&lt;210&gt; 328

&lt;211&gt; 498

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 328

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Met Phe Asn Tyr Glu Arg Pro Lys His Phe Ile Gln Ser Gln Asn Pro
1           5           10           15
Cys Gly Ser Arg Leu Gln Pro Pro Gly Pro Glu Thr Ser Ser Phe Ser
20           25           30
Ser Gln Thr Lys Gln Ser Ser Ile Ile Ile Gln Pro Arg Gln Cys Thr
35           40           45
Glu Gln Arg Phe Ser Ala Ser Ser Thr Leu Ser Ser His Ile Thr Met
50           55           60
Ser Ser Ser Ala Phe Pro Ala Ser Pro Gln Gln His Ala Gly Ser Asn
65           70           75           80
Pro Gly Gln Arg Val Thr Thr Thr Tyr Asn Gln Ser Pro Ala Ser Phe
85           90           95

```

338

Leu Ser Ser Ile Leu Pro Ser Gln Pro Asp Tyr Asn Ser Ser Lys Ile  
 100 105 110  
 Pro Ser Ala Met Asp Ser Asn Tyr Gln Gln Ser Ser Ala Gly Gln Pro  
 115 120 125  
 Ile Asn Ala Lys Pro Ser Gln Thr Ala Asn Ala Lys Pro Ile Pro Arg  
 130 135 140  
 Thr Pro Asp His Glu Ile Gln Gly Ser Lys Glu Ala Leu Ile Gln Asp  
 145 150 155 160  
 Leu Glu Arg Lys Leu Lys Cys Lys Asp Thr Leu Leu His Asn Gly Asn  
 165 170 175  
 Gln Arg Leu Thr Tyr Glu Glu Lys Met Ala Arg Arg Leu Leu Gly Pro  
 180 185 190  
 Gln Asn Ala Ala Ala Val Phe Gln Ala Gln Asp Asp Ser Gly Ala Gln  
 195 200 205  
 Asp Ser Gln Gln His Asn Ser Glu His Ala Arg Leu Gln Val Pro Thr  
 210 215 220  
 Ser Gln Val Arg Ser Arg Ser Thr Ser Arg Gly Asp Val Asn Asp Gln  
 225 230 235 240  
 Asp Ala Ile Gln Glu Lys Phe Tyr Pro Pro Arg Phe Ile Gln Val Pro  
 245 250 255  
 Glu Asn Met Ser Ile Asp Glu Gly Arg Phe Cys Arg Met Asp Phe Lys  
 260 265 270  
 Val Ser Gly Leu Pro Ala Pro Asp Val Ser Trp Tyr Leu Asn Gly Arg  
 275 280 285  
 Thr Val Gln Ser Asp Asp Leu His Lys Met Ile Val Ser Glu Lys Gly  
 290 295 300  
 Leu His Ser Leu Ile Phe Glu Val Val Arg Ala Ser Asp Ala Gly Ala  
 305 310 315 320  
 Tyr Ala Cys Val Ala Lys Asn Arg Ala Gly Glu Ala Thr Phe Thr Val  
 325 330 335  
 Gln Leu Asp Val Leu Ala Lys Glu His Lys Arg Ala Pro Met Phe Ile  
 340 345 350  
 Tyr Lys Pro Gln Ser Lys Lys Val Leu Glu Gly Asp Ser Val Lys Leu  
 355 360 365  
 Glu Cys Gln Ile Ser Ala Ile Pro Pro Pro Lys Leu Phe Trp Lys Arg  
 370 375 380  
 Asn Asn Glu Met Val Gln Phe Asn Thr Asp Arg Ile Ser Leu Tyr Gln  
 385 390 395 400  
 Asp Asn Thr Gly Arg Val Thr Leu Leu Ile Lys Asp Val Asn Lys Lys  
 405 410 415  
 Asp Ala Gly Trp Tyr Thr Val Ser Ala Val Asn Glu Ala Gly Val Thr  
 420 425 430  
 Thr Cys Asn Thr Arg Leu Asp Val Thr Ala Arg Pro Asn Gln Thr Leu  
 435 440 445  
 Pro Ala Pro Lys Gln Leu Arg Val Arg Pro Thr Phe Ser Lys Tyr Leu  
 450 455 460  
 Ala Leu Asn Gly Lys Gly Leu Asn Val Lys Gln Ala Phe Asn Pro Glu  
 465 470 475 480  
 Gly Glu Phe Gln Arg Leu Ala Ala Gln Ser Gly Leu Tyr Glu Ser Glu  
 485 490 495  
 Glu Leu

&lt;210&gt; 329

&lt;211&gt; 3649

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 329

aattttctccg	taattttccac	tgcttgaagg	ctgctcgagg	aacaggagca	gcggcgaaac	60
ccaggtctgt	cggtttacga	gaatgcagtt	tccaagtacg	gctctcagtt	ccaaggcaat	120
tcccagcacg	acgccctgga	attcctgctc	tggttgctgg	atcgtgtaca	tgaggacctg	180
gagggttcat	cccaggggcc	ggtgtcggag	aagcttccgc	ctgaagccac	taaaacctct	240
gagaactgcc	tgtcaccatc	agctcagctt	cctctaggtc	aaagctttgt	gcaaagccac	300
tttcaagcac	aatatagatc	ttccttgact	tgtccccact	gcctgaaaca	gagcaacacc	360
tttgatcett	tcctgtgtgt	gtccctacct	atccccctgc	gccagacgag	gttcttgagt	420
gtcaccctgg	tcttcccctc	taagagccag	cggttcctgc	gggttggcct	ggccgtgccg	480
atcctcagca	cagtggcagc	cctgaggaag	atggttgagc	aggaaggagg	cgtccctgca	540
gatgaggtga	tcttggttga	actgtatccc	agtggattcc	agcgggtctt	ctttgatgaa	600
gaggacctga	ataccatcgc	agagggagat	aatgtgtatg	cctttcaagt	tcctccctca	660
cccagccagg	ggactctctc	agctcatcca	ctgggtctgt	cgccctcccc	acgcctggca	720
gcccgtagag	gccagcgatt	ctccctctct	ctccacagtg	agagcaaggt	gctaatactc	780
ttctgtaact	tggtgggggc	agggcagcag	gctagcaggt	ttgggccacc	cttcctgata	840
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gtgggactct	ctgtggcctg	cagctatctg	tctccgaagg	acagtcggcc	cctctgtcac	1020
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caggttcctg	actctcccat	cttcaccaac	agcctctgca	atcaggaaaa	gggaggggtg	1920
gagcccaggc	gttttggtacg	gggcgtgaaa	ggcagaagca	ttagcatgaa	ggcaccaccc	1980
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cctcggtcca	cgagccagtc	cattgtgtcg	ctggtgacgg	gcactgcggg	tgaggatgag	2160
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gtgtttcgga	agaaggagaa	caggaggaat	gagagggcag	aggtctctcc	acaggtgccc	2640
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agcttttgat	ggagcgtgtc	agtattgtgt	gacgctggca	ttcttgggac	tttgccaagc	3000
aactgtaggc	agctcatgtt	gagaatgggt	ttccaggaaa	cccgttgtct	tgtaatctct	3060
aaaaaaaaat	tttttttttt	ttgtggtggg	gggtctccat	atctagactt	ccaacaccca	3120
aggtccatat	taaaaaaggt	cgaaaaacct	cctgcacatc	tggttgcttt	gctacagttt	3180
ggccactaga	ggatgctatt	gggtcagtat	taccagtttc	agggcaagaa	ctgatattta	3240
ctaaagagtt	ttggatgtgg	gcaaacaaga	tgaggctggg	ttaataagaa	tcttcaatgt	3300
cgtgtcaaat	actgtcaatg	gcttttccct	tttctttctt	ttttttttta	attgtggact	3360

340

taaagaaaaa tattttattt ttaatgcttt tctgggataa gcattaaaga tgccaaaaag 3420  
 aaaaaaaaac aaaagaatga tagtgatggt aaggcaagat tctagcaaag agagatggga 3480  
 gataaatggc tgagagttca ggtgaatatt taatatatta aaaattgtat taaagttttt 3540  
 caaggtattt taaaaataac tattttgata ctagaaaaaa agtccatttt ttaattttaa 3600  
 tatgagatct atgtacaatt ttaataaaat cctgtccatg aaacacgca 3649

&lt;210&gt; 330

&lt;211&gt; 812

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 330

Met	Val	Ala	Glu	Glu	Gly	Gly	Val	Pro	Ala	Asp	Glu	Val	Ile	Leu	Val
1				5				10						15	
Glu	Leu	Tyr	Pro	Ser	Gly	Phe	Gln	Arg	Ser	Phe	Phe	Asp	Glu	Glu	Asp
		20					25					30			
Leu	Asn	Thr	Ile	Ala	Glu	Gly	Asp	Asn	Val	Tyr	Ala	Phe	Gln	Val	Pro
	35						40				45				
Pro	Ser	Pro	Ser	Gln	Gly	Thr	Leu	Ser	Ala	His	Pro	Leu	Gly	Leu	Ser
	50				55						60				
Ala	Ser	Pro	Arg	Leu	Ala	Ala	Arg	Glu	Gly	Gln	Arg	Phe	Ser	Leu	Ser
65				70				75						80	
Leu	His	Ser	Glu	Ser	Lys	Val	Leu	Ile	Leu	Phe	Cys	Asn	Leu	Val	Gly
			85				90						95		
Ser	Gly	Gln	Gln	Ala	Ser	Arg	Phe	Gly	Pro	Pro	Phe	Leu	Ile	Arg	Glu
	100						105					110			
Asp	Arg	Ala	Val	Ser	Trp	Ala	Gln	Leu	Gln	Gln	Ser	Ile	Leu	Ser	Lys
	115						120				125				
Val	Arg	His	Leu	Met	Lys	Ser	Glu	Ala	Pro	Val	Gln	Asn	Leu	Gly	Ser
	130				135						140				
Leu	Phe	Ser	Ile	Arg	Val	Val	Gly	Leu	Ser	Val	Ala	Cys	Ser	Tyr	Leu
145				150				155						160	
Ser	Pro	Lys	Asp	Ser	Arg	Pro	Leu	Cys	His	Trp	Ala	Val	Asp	Arg	Val
			165				170						175		
Leu	His	Leu	Arg	Arg	Pro	Gly	Gly	Pro	Pro	His	Val	Lys	Leu	Ala	Val
	180						185						190		
Glu	Trp	Asp	Ser	Ser	Val	Lys	Glu	Arg	Leu	Phe	Gly	Ser	Leu	Gln	Glu
	195						200					205			
Glu	Arg	Ala	Gln	Asp	Ala	Asp	Ser	Val	Trp	Gln	Gln	Gln	Gln	Ala	His
	210				215						220				
Gln	Gln	His	Ser	Cys	Thr	Leu	Asp	Glu	Cys	Phe	Gln	Phe	Tyr	Thr	Lys
225				230				235						240	
Glu	Glu	Gln	Leu	Ala	Gln	Asp	Asp	Ala	Trp	Lys	Cys	Pro	His	Cys	Gln
			245					250					255		
Val	Leu	Gln	Gln	Gly	Met	Val	Lys	Leu	Ser	Leu	Trp	Thr	Leu	Pro	Asp
	260						265						270		
Ile	Leu	Ile	Ile	His	Leu	Lys	Arg	Phe	Cys	Gln	Val	Gly	Glu	Arg	Arg
	275						280					285			
Asn	Lys	Leu	Ser	Thr	Leu	Val	Lys	Phe	Pro	Leu	Ser	Gly	Leu	Asn	Met
	290				295						300				
Ala	Pro	His	Val	Ala	Gln	Arg	Ser	Thr	Ser	Pro	Glu	Ala	Gly	Leu	Gly
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Pro	Trp	Pro	Ser	Trp	Lys	Gln	Pro	Asp	Cys	Leu	Pro	Thr	Ser	Tyr	Pro
			325					330						335	
Leu	Asp	Phe	Leu	Tyr	Asp	Leu	Tyr	Ala	Val	Cys	Asn	His	His	Gly	Asn
		340					345					350			
Leu	Gln	Gly	Gly	His	Tyr	Thr	Ala	Tyr	Cys	Arg	Asn	Ser	Leu	Asp	Gly
	355						360					365			



341

Gln Trp Tyr Ser Tyr Asp Asp Ser Thr Val Glu Pro Leu Arg Glu Asp  
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 Glu Val Asn Thr Arg Gly Ala Tyr Ile Leu Phe Tyr Gln Lys Arg Asn  
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 405 410 415  
 Ser Ser Leu Ser Asp His Trp Leu Leu Arg Leu Gly Ser His Ala Gly  
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 690 695 700  
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 Pro Glu Gly Leu Ala Arg Gly Leu Gly Ser Arg Leu Glu Arg Asp Val  
 740 745 750  
 Trp Ser Ala Pro Ser Ser Leu Arg Leu Pro Arg Lys Ala Ser Arg Ala  
 755 760 765  
 Pro Arg Gly Ser Ala Leu Gly Met Ser Gln Arg Thr Val Pro Gly Glu  
 770 775 780  
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342

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 <213> Homo sapiens

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 <212> PRT  
 <213> Homo sapiens

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 20 25 30  
 Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile  
 35 40 45  
 Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu  
 50 55 60  
 Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val  
 65 70 75 80  
 His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met  
 85 90 95  
 Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn  
 100 105 110

343

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr  
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 Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu  
 130 135 140  
 Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn  
 145 150 155 160  
 Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln  
 165 170 175  
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 180 185 190  
 Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met  
 195 200 205  
 Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser  
 210 215 220  
 Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val  
 225 230 235 240  
 Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser  
 245 250 255  
 Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu  
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 Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys  
 275 280

&lt;210&gt; 333

&lt;211&gt; 1984

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 333

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344

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&lt;210&gt; 334

&lt;211&gt; 258

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 334

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Pro	Ser	Met	Lys	Asn	Ile	Asn	Pro	Leu	Thr	Ala	Met	Ser	Tyr	Leu	Arg
			20					25					30		
Lys	Leu	Asp	Thr	Ser	Gly	Phe	Ser	Ser	Ile	Leu	Val	Thr	Leu	Thr	Lys
		35					40					45			
Ala	Ala	Val	Ala	Leu	Lys	Met	Gly	Asp	Leu	Asp	Met	His	Arg	Asn	Glu
		50				55					60				
Met	Lys	Ser	His	Ser	Glu	Met	Lys	Leu	Val	Cys	Gly	Phe	Ile	Leu	Glu
65					70					75				80	
Pro	Arg	Leu	Leu	Ile	Gln	Gln	Arg	Lys	Gly	Gln	Ile	Val	Pro	Thr	Glu
				85					90					95	
Leu	Ala	Leu	His	Leu	Lys	Glu	Thr	Gln	Pro	Gly	Leu	Leu	Val	Ala	Ser
			100					105					110		
Val	Leu	Gly	Leu	Gln	Lys	Asn	Asn	Lys	Ile	Gly	Ile	Glu	Glu	Ala	Asp
		115					120					125			
Ser	Phe	Phe	Lys	Val	Leu	Cys	Ala	Lys	Asp	Glu	Asp	Thr	Ile	Pro	Gln
		130				135					140				
Leu	Leu	Val	Asp	Phe	Trp	Glu	Ala	Gln	Leu	Val	Ala	Cys	Leu	Pro	Asp
145					150					155				160	
Val	Val	Leu	Gln	Glu	Leu	Phe	Phe	Lys	Leu	Thr	Ser	Gln	Tyr	Ile	Trp
			165						170					175	
Arg	Leu	Ser	Lys	Arg	Gln	Pro	Pro	Asp	Thr	Thr	Pro	Leu	Arg	Thr	Ser
			180					185					190		
Glu	Asp	Leu	Ile	Asn	Ala	Cys	Ser	His	Tyr	Gly	Leu	Ile	Tyr	Pro	Trp
		195					200					205			
Val	His	Val	Val	Ile	Ser	Ser	Asp	Ser	Leu	Ala	Asp	Lys	Asn	Tyr	Thr
		210					215				220				
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His Ala

&lt;210&gt; 335

&lt;211&gt; 2180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2180)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 335

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&lt;210&gt; 336

&lt;211&gt; 234

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 336

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Pro Ala Gly Ser Gly Leu Ser Ala Ser Gln Arg Arg Ala Glu Leu Arg
20          25          30
Arg Arg Lys Leu Leu Met Asn Ser Glu Gln Arg Ile Asn Arg Ile Met
35          40          45
Gly Phe His Arg Pro Gly Ser Gly Ala Glu Glu Glu Ser Gln Thr Lys
50          55          60
Ser Lys Gln Gln Asp Ser Asp Lys Leu Asn Ser Leu Ser Val Pro Ser
65          70          75          80
Val Ser Lys Arg Val Val Leu Gly Asp Ser Val Ser Thr Gly Thr Thr
85          90          95

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346

Asp Gln Gln Gly Gly Val Ala Glu Val Lys Gly Thr Gln Leu Gly Asp  
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 115 120 125  
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 130 135 140  
 Gln Arg Gly Ser Arg His Gly Leu Glu Gln Tyr Leu Ser Arg Phe Glu  
 145 150 155 160  
 Glu Ala Met Lys Leu Arg Lys Gln Leu Ile Ser Glu Lys Pro Ser Gln  
 165 170 175  
 Glu Asp Gly Asn Thr Thr Glu Glu Phe Asp Ser Phe Arg Ile Phe Arg  
 180 185 190  
 Leu Val Gly Cys Ala Leu Leu Ala Leu Gly Val Arg Ala Phe Val Cys  
 195 200 205  
 Lys Tyr Leu Ser Ile Phe Ala Pro Phe Leu Thr Leu Gln Leu Ala Leu  
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 <213> Homo sapiens

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&lt;210&gt; 338

&lt;211&gt; 353

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

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          20          25          30
Val Leu Cys Val Gly Thr Phe Phe Cys Leu Phe Ile Phe Phe Ser Asn
          35          40          45
Ser Leu Val Ile Ala Ala Val Ile Lys Asn Arg Lys Phe His Phe Pro
          50          55          60
Phe Tyr Tyr Leu Leu Ala Asn Leu Ala Ala Asp Phe Phe Ala Gly
          65          70          75          80
Ile Ala Tyr Val Phe Leu Met Phe Asn Thr Gly Pro Val Ser Lys Thr
          85          90          95
Leu Thr Val Asn Arg Trp Phe Leu Arg Gln Gly Leu Leu Asp Ser Ser
          100         105         110
Leu Thr Ala Ser Leu Thr Asn Leu Leu Val Ile Ala Val Glu Arg His
          115         120         125
Met Ser Ile Met Arg Met Arg Val His Ser Asn Leu Thr Lys Lys Arg
          130         135         140
Val Thr Leu Leu Ile Leu Leu Val Trp Ala Ile Ala Ile Phe Met Gly
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348

[illegible]

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<211> 3320
<212> DNA
<213> Homo sapiens
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349

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&lt;210&gt; 340

&lt;211&gt; 784

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 340

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Met Gly Ser Thr Asp Ser Lys Leu Asn Phe Arg Lys Ala Val Ile Gln
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Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
          20          25          30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
          35          40          45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
          50          55          60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
          65          70          75          80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
          85          90          95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
          100         105         110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
          115         120         125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
          130         135         140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Thr Gln Ser
          145         150         155         160

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350

His	Arg	Arg	Ser	Thr	Val	Asp	Ser	Ala	Glu	Asp	Val	His	Ser	Leu	Asp	165	170	175
Ser	Cys	Glu	Tyr	Ile	Trp	Glu	Ala	Gly	Val	Gly	Phe	Ala	His	Ser	Pro	180	185	190
Gln	Pro	Asn	Tyr	Ile	His	Asp	Met	Asn	Arg	Met	Glu	Leu	Leu	Lys	Leu	195	200	205
Leu	Leu	Thr	Cys	Phe	Ser	Glu	Ala	Met	Tyr	Leu	Pro	Pro	Ala	Pro	Glu	210	215	220
Ser	Gly	Ser	Thr	Asn	Pro	Trp	Val	Gln	Phe	Phe	Cys	Ser	Thr	Glu	Asn	225	230	235
Arg	His	Ala	Leu	Pro	Leu	Phe	Thr	Ser	Leu	Leu	Asn	Thr	Val	Cys	Ala	245	250	255
Tyr	Asp	Pro	Val	Gly	Tyr	Gly	Ile	Pro	Tyr	Asn	His	Leu	Leu	Phe	Ser	260	265	270
Asp	Tyr	Arg	Glu	Pro	Leu	Val	Glu	Ala	Gln	Val	Leu	Ile	Val	Thr	Leu	275	280	285
Asp	His	Asp	Ser	Ala	Ser	Ser	Ala	Ser	Pro	Thr	Val	Asp	Gly	Thr	Thr	290	295	300
Thr	Gly	Thr	Ala	Met	Asp	Asp	Ala	Asp	Pro	Pro	Gly	Pro	Glu	Asn	Leu	305	310	315
Phe	Val	Asn	Tyr	Leu	Ser	Arg	Ile	His	Arg	Glu	Glu	Asp	Phe	Gln	Phe	325	330	335
Ile	Leu	Lys	Gly	Ile	Ala	Arg	Leu	Leu	Ser	Asn	Pro	Leu	Leu	Gln	Thr	340	345	350
Tyr	Leu	Pro	Asn	Ser	Thr	Lys	Lys	Ile	Gln	Phe	His	Gln	Glu	Leu	Leu	355	360	365
Val	Leu	Phe	Trp	Lys	Leu	Cys	Asp	Phe	Asn	Lys	Lys	Phe	Leu	Phe	Phe	370	375	380
Val	Leu	Lys	Ser	Ser	Asp	Val	Leu	Asp	Ile	Leu	Val	Pro	Ile	Leu	Phe	385	390	395
Phe	Leu	Asn	Asp	Ala	Arg	Ala	Asp	Gln	Ser	Arg	Val	Gly	Leu	Met	His	405	410	415
Ile	Gly	Val	Phe	Ile	Leu	Leu	Leu	Leu	Ser	Gly	Glu	Arg	Asn	Phe	Gly	420	425	430
Val	Arg	Leu	Asn	Lys	Pro	Tyr	Ser	Ile	Arg	Val	Pro	Met	Asp	Ile	Pro	435	440	445
Val	Phe	Thr	Gly	Thr	His	Ala	Asp	Leu	Leu	Ile	Val	Val	Phe	His	Lys	450	455	460
Ile	Ile	Thr	Ser	Gly	His	Gln	Arg	Leu	Gln	Pro	Leu	Phe	Asp	Cys	Leu	465	470	475
Leu	Thr	Ile	Val	Val	Asn	Val	Ser	Pro	Tyr	Leu	Lys	Ser	Leu	Ser	Met	485	490	495
Val	Thr	Ala	Asn	Lys	Leu	Leu	His	Leu	Leu	Glu	Ala	Phe	Ser	Thr	Thr	500	505	510
Trp	Phe	Leu	Phe	Ser	Ala	Ala	Gln	Asn	His	His	Leu	Val	Phe	Phe	Leu	515	520	525
Leu	Glu	Val	Phe	Asn	Asn	Ile	Ile	Gln	Tyr	Gln	Phe	Asp	Gly	Asn	Ser	530	535	540
Asn	Leu	Val	Tyr	Ala	Ile	Ile	Arg	Lys	Arg	Ser	Ile	Phe	His	Gln	Leu	545	550	555
Ala	Asn	Leu	Pro	Thr	Asp	Pro	Pro	Thr	Ile	His	Lys	Ala	Leu	Gln	Arg	565	570	575
Arg	Arg	Arg	Thr	Pro	Glu	Pro	Leu	Ser	Arg	Thr	Gly	Ser	Gln	Glu	Gly	580	585	590
Thr	Ser	Met	Glu	Gly	Ser	Arg	Pro	Ala	Ala	Pro	Ala	Glu	Pro	Gly	Thr	595	600	605
Leu	Lys	Thr	Ser	Leu	Val	Ala	Thr	Pro	Gly	Ile	Asp	Lys	Leu	Thr	Glu	610	615	620

351

Lys Ser Gln Val Ser Glu Asp Gly Thr Leu Arg Ser Leu Glu Pro Glu  
 625 630 635 640  
 Pro Gln Gln Ser Leu Glu Asp Gly Ser Pro Ala Lys Gly Glu Pro Ser  
 645 650 655  
 Gln Ala Trp Arg Glu Gln Arg Arg Pro Ser Thr Ser Ser Ala Ser Gly  
 660 665 670  
 Gln Trp Ser Pro Thr Pro Glu Trp Val Leu Ser Trp Lys Ser Lys Leu  
 675 680 685  
 Pro Leu Gln Thr Ile Met Arg Leu Leu Gln Val Leu Val Pro Gln Val  
 690 695 700  
 Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu Ser Glu Ile Leu  
 705 710 715 720  
 Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu Pro Val Pro His  
 725 730 735  
 Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly Thr Ala Met Trp  
 740 745 750  
 Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg Asn Val Asp Pro  
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 <212> DNA  
 <213> Homo sapiens

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&lt;210&gt; 342

&lt;211&gt; 788

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 342

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Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
20     25     30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
35     40     45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
50     55     60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
65     70     75     80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
85     90     95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
100    105    110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
115    120    125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
130    135    140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Phe Thr Val
145    150    155    160
Gln Ser His Arg Arg Ser Thr Val Asp Ser Ala Glu Asp Val His Ser
165    170    175
Leu Asp Ser Cys Glu Tyr Ile Trp Glu Ala Gly Val Gly Phe Ala His
180    185    190
Ser Pro Gln Pro Asn Tyr Ile His Asp Met Asn Arg Met Glu Leu Leu

```

	195					200					205				
Lys 210	Leu	Leu	Thr		Cys	Phe 215	Ser	Glu	Ala	Met	Tyr 220	Leu	Pro	Pro	Ala
Pro 225	Glu	Ser	Gly	Ser	Thr 230	Asn	Pro	Trp	Val	Gln 235	Phe	Phe	Cys	Ser	Thr 240
Glu	Asn	Arg	His	Ala 245	Leu	Pro	Leu	Phe	Thr 250	Ser	Leu	Leu	Asn	Thr	Val 255
Cys	Ala	Tyr	Asp 260	Pro	Val	Gly	Tyr	Gly 265	Ile	Pro	Tyr	Asn	His	Leu	Leu 270
Phe	Ser	Asp 275	Tyr	Arg	Glu	Pro	Leu	Val 280	Glu	Glu	Ala	Ala	Gln	Val	Leu 285
Ile 290	Val	Thr	Leu	Asp	His	Asp 295	Ser	Ala	Ser	Ser	Ala	Ser	Pro	Thr	Val 300
Asp 305	Gly	Thr	Thr	Thr	Gly 310	Thr	Ala	Met	Asp	Asp	Ala	Asp	Pro	Pro	Gly 320
Pro	Glu	Asn	Leu	Phe 325	Val	Asn	Tyr	Leu	Ser	Arg 330	Ile	His	Arg	Glu	Glu 335
Asp	Phe	Gln	Phe 340	Ile	Leu	Lys	Gly	Ile 345	Ala	Arg	Leu	Leu	Ser	Asn	Pro 350
Leu	Leu	Gln 355	Thr	Tyr	Leu	Pro	Asn	Ser 360	Thr	Lys	Lys	Ile	Gln	Phe	His 365
Gln	Glu	Leu 370	Leu	Val	Leu	Phe	Trp	Lys 375	Leu	Cys	Asp	Phe	Asn	Lys	Lys 380
Phe 385	Leu	Phe	Phe	Val	Leu 390	Lys	Ser	Ser	Asp	Val	Leu	Asp	Ile	Leu	Val 400
Pro	Ile	Leu	Phe 405	Phe	Leu	Asn	Asp	Ala	Arg 410	Ala	Asp	Gln	Ser	Arg	Val 415
Gly	Leu	Met	His 420	Ile	Gly	Val	Phe	Ile 425	Leu	Leu	Leu	Leu	Ser	Gly	Glu 430
Arg	Asn	Phe 435	Gly	Val	Arg	Leu	Asn	Lys 440	Pro	Tyr	Ser	Ile	Arg	Val	Pro 445
Met	Asp 450	Ile	Pro	Val	Phe	Thr	Gly	Thr 455	His	Ala	Asp	Leu	Leu	Ile	Val 460
Val 465	Phe	His	Lys	Ile	Ile	Thr	Ser	Gly 470	His	Gln	Arg	Leu	Gln	Pro	Leu 480
Phe	Asp	Cys	Leu	Leu 485	Thr	Ile	Val	Val 490	Asn	Val	Ser	Pro	Tyr	Leu	Lys 495
Ser	Leu	Ser	Met 500	Val	Thr	Ala	Asn	Lys 505	Leu	Leu	His	Leu	Leu	Glu	Ala 510
Phe	Ser	Thr 515	Thr	Trp	Phe	Leu	Phe	Ser 520	Ala	Ala	Gln	Asn	His	His	Leu 525
Val	Phe 530	Phe	Leu	Leu	Glu	Val	Phe	Asn 535	Asn	Ile	Ile	Gln	Tyr	Gln	Phe 540
Asp 545	Gly	Asn	Ser	Asn	Leu	Val	Tyr	Ala 550	Ile	Ile	Arg	Lys	Arg	Ser	Ile 560
Phe	His	Gln	Leu	Ala 565	Asn	Leu	Pro	Thr	Asp	Pro	Pro	Thr	Ile	His	Lys 575
Ala	Leu	Gln	Arg 580	Arg	Arg	Arg	Thr	Pro 585	Glu	Pro	Leu	Ser	Arg	Thr	Gly 590
Ser	Gln	Glu 595	Gly	Thr	Ser	Met	Glu	Gly 600	Ser	Arg	Pro	Ala	Ala	Pro	Ala 605
Glu	Pro 610	Gly	Thr	Leu	Lys	Thr	Ser	Leu 615	Val	Ala	Thr	Pro	Gly	Ile	Asp 620
Lys 625	Leu	Thr	Glu	Lys	Ser	Gln	Val	Ser 630	Glu	Asp	Gly	Thr	Leu	Arg	Ser 640
Leu	Glu	Pro	Glu	Pro 645	Gln	Gln	Ser	Leu 650	Glu	Asp	Gly	Ser	Pro	Ala	Lys 655
Gly	Glu	Pro	Ser	Gln	Ala	Trp	Arg	Glu	Gln	Arg	Arg	Pro	Ser	Thr	Ser

354

	660		665		670
Ser Ala	Ser Gly Gln Trp Ser	Pro Thr Pro Glu Trp	Val Leu Ser Trp		
	675	680	685		
Lys Ser	Lys Leu Pro Leu Gln Thr	Ile Met Arg Leu Leu	Gln Val Leu		
	690	695	700		
Val Pro	Gln Val Glu Lys Ile Cys Ile	Asp Lys Gly Leu Thr	Asp Glu		
705		710	715		720
Ser Glu	Ile Leu Arg Phe Leu Gln His	Gly Thr Leu Val Gly	Leu Leu		
	725	730	735		
Pro Val	Pro His Pro Ile Leu Ile	Arg Lys Tyr Gln Ala	Asn Ser Gly		
	740	745	750		
Thr Ala	Met Trp Phe Arg Thr Tyr	Met Trp Gly Val Ile	Tyr Leu Arg		
	755	760	765		
Asn Val	Asp Pro Pro Val Trp Tyr	Asp Thr Asp Val Lys	Leu Phe Glu		
	770	775	780		
Ile Gln	Arg Val				
785					

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 <211> 563  
 <212> DNA  
 <213> Homo sapiens

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 ctgcagtaaa agctggagga atgagaattt ccaaaaaaca agaaattggc accttgaaa 180  
 gacataccaa aaaaacagga ttcgagaaaa caagtgccat tgcaaatgtt gccaaaatac 240  
 agacactgga tgccctgaat gacgcactgg agaagctcaa ctataaattt ccagcaacag 300  
 tgcacatggc gcatcaaaaa cccacacctg ctctggaaaa gggtgttcca ctgaaaagga 360  
 tctacattat tcagcagcct cgaaaatgtt aagcctggat ttaaaacaca gccgtctggc 420  
 cagctgcctc gaatatctga cagcttagca aaaagggcca aagctttcca taggcgtgct 480  
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 catccaaact tgtaaaaaaa aaa 563

<210> 344  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 344  
 Met Ala Asn Glu Val Gln Asp Leu Leu Ser Pro Arg Lys Gly Gly His  
 1 5 10 15  
 Pro Pro Ala Val Lys Ala Gly Gly Met Arg Ile Ser Lys Lys Gln Glu  
 20 25 30  
 Ile Gly Thr Leu Glu Arg His Thr Lys Lys Thr Gly Phe Glu Lys Thr  
 35 40 45  
 Ser Ala Ile Ala Asn Val Ala Lys Ile Gln Thr Leu Asp Ala Leu Asn  
 50 55 60  
 Asp Ala Leu Glu Lys Leu Asn Tyr Lys Phe Pro Ala Thr Val His Met  
 65 70 75 80  
 Ala His Gln Lys Pro Thr Pro Ala Leu Glu Lys Val Val Pro Leu Lys  
 85 90 95  
 Arg Ile Tyr Ile Ile Gln Gln Pro Arg Lys Cys  
 100 105

<210> 345  
 <211> 3733  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(3733)  
 <223> n = A,T,C or G

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 gaagcgtcca aagagggacg gctgtcagcc ctgcttgact gagaaccac cagctcatcc 120  
 cagacacctc atagcaacct atttatacaa agggggaaag aaacacctga gcagaatgga 180  
 atcattatct ttttcccaag gagaaaaccg gggtaaaggg agggaagcaa ttcaatttgg 240  
 agtccctgtg aatgggcttt cagaaggcaa ttaaagaaat ccactcagag aggacttggg 300  
 gtgaaacttg ggtcctgttg ttttctgatt gtaagtggaa gcaggtcttg cacacgctgt 360  
 tggcaaagtgt caggaccagg ttaagtgact ggcagaaaaa cttccagggtg gaacaagcaa 420  
 cccaggttct gctgcaagct tgaaggagcc tggagcggga gaaagctaac ttgaacatga 480  
 cctgttgcat ttggcaagtt cttagcaacat gctcctaagg aagcgataca ggcacagacc 540  
 atgcagactc cagttcctcc tgctgctcct gatgctggga tgcgtcctga tgatggtggc 600  
 gatgttgca cctccccacc acaccctgca ccagactgtc acagcccaag ccagcaagca 660  
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 tgaggatgag ggtgaagagt acagccctct ggagggcctg ccacccttta tctcactgcg 780  
 ggaggatcag ctgctggttg ccgtggcctt accccaggcc agaaggaacc agagccaggg 840  
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 ggctctgccc gaggtgcggc acccactgtg tctgcagcag caccctcagg acagcctgcc 1080  
 cacagccagc gtcactctct gtttccatga tgagggcctg tccactctcc tgcggactgt 1140  
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 caccagagcc accggggatg tgctcgtctt catggatgcc cactgcgagt gccaccagg 1380  
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 gatagatgtg attgactgga agactttcca gtattacccc tcaaaggacc tgcagcgtgg 1500  
 ggtgttgagc tggaagctgg atttccactg ggaacctttg ccagagcatg tgaggaagc 1560  
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 tctttgtttt tctccactga gcaacttaaca attgncttct tctctggcct ggacattctc 2760  
 tggcagcacc tccaggatac ataaattcaa tggatcaatt tatttgtctt caaatggcct 2820

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taacttggat tgtctgtttg gccaacccatg aaaattaaag agtctaagca gatgtaatgg 2880
cctgacattc caaaaactct gaattgggtt tattagcaca aatgttgtgt tcatttgttg 2940
agccatatct cagaangaag gaaangggna gctacagaaa nggaggttta ggattgcaga 3000
gaangatgca agnagcactt tggcccaatt ctccnagctn caaccagca gctgaaaagc 3060
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gaacctttct gggncctgtg tacagggttg cactgctgga gcanaacaca cttttttnaa 3660
aaagcaaacc tttttctggg gaggnaaagc caaaactggg ccaaantttt tgacnggaaa 3720
atttgggggt aag 3733

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&lt;210&gt; 346

&lt;211&gt; 639

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 346

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Met Leu Leu Arg Lys Arg Tyr Arg His Arg Pro Cys Arg Leu Gln Phe
 1          5          10          15
Leu Leu Leu Leu Leu Met Leu Gly Cys Val Leu Met Met Val Ala Met
 20          25          30
Leu His Pro Pro His His Thr Leu His Gln Thr Val Thr Ala Gln Ala
 35          40          45
Ser Lys His Ser Pro Glu Ala Arg Tyr Arg Leu Asp Phe Gly Glu Ser
 50          55          60
Gln Asp Trp Val Leu Glu Ala Glu Asp Glu Gly Glu Glu Tyr Ser Pro
 65          70          75          80
Leu Glu Gly Leu Pro Pro Phe Ile Ser Leu Arg Glu Asp Gln Leu Leu
 85          90          95
Val Ala Val Ala Leu Pro Gln Ala Arg Arg Asn Gln Ser Gln Gly Arg
100          105          110
Arg Gly Gly Ser Tyr Arg Leu Ile Lys Gln Pro Arg Arg Gln Asp Lys
115          120          125
Glu Ala Pro Lys Arg Asp Trp Gly Ala Asp Glu Asp Gly Glu Val Ser
130          135          140
Glu Glu Glu Glu Leu Thr Pro Phe Ser Leu Asp Pro Arg Gly Leu Gln
145          150          155          160
Glu Ala Leu Ser Ala Arg Ile Pro Leu Gln Arg Ala Leu Pro Glu Val
165          170          175
Arg His Pro Leu Cys Leu Gln Gln His Pro Gln Asp Ser Leu Pro Thr
180          185          190
Ala Ser Val Ile Leu Cys Phe His Asp Glu Ala Trp Ser Thr Leu Leu
195          200          205
Arg Thr Val His Ser Ile Leu Asp Thr Val Pro Arg Ala Phe Leu Lys
210          215          220
Glu Ile Ile Leu Val Asp Asp Leu Ser Gln Gln Gly Gln Leu Lys Ser
225          230          235          240
Ala Leu Ser Glu Tyr Val Ala Arg Leu Glu Gly Val Lys Leu Leu Arg
245          250          255
Ser Asn Lys Arg Leu Gly Ala Ile Arg Ala Arg Met Leu Gly Ala Thr
260          265          270
Arg Ala Thr Gly Asp Val Leu Val Phe Met Asp Ala His Cys Glu Cys

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357

275	280	285
His Pro Gly Trp Leu Glu Pro	Leu Leu Ser Arg Ile Ala Gly Asp Arg	
290	295	300
Ser Arg Val Val Ser Pro Val	Ile Asp Val Ile Asp Trp Lys Thr Phe	
305	310	315
Gln Tyr Tyr Pro Ser Lys Asp	Leu Gln Arg Gly Val Leu Asp Trp Lys	
325	330	335
Leu Asp Phe His Trp Glu Pro	Leu Pro Glu His Val Arg Lys Ala Leu	
340	345	350
Gln Ser Pro Ile Ser Pro Ile	Arg Ser Pro Val Val Pro Gly Glu Val	
355	360	365
Val Ala Met Asp Arg His Tyr	Phe Gln Asn Thr Gly Ala Tyr Asp Ser	
370	375	380
Leu Met Ser Leu Arg Gly Gly	Glu Asn Leu Glu Leu Ser Phe Lys Ala	
385	390	395
Trp Leu Cys Gly Gly Ser Val	Glu Ile Leu Pro Cys Ser Arg Val Gly	
405	410	415
His Ile Tyr Gln Asn Gln Asp	Ser His Ser Pro Leu Asp Gln Glu Ala	
420	425	430
Thr Leu Arg Asn Arg Val Arg	Ile Ala Glu Thr Trp Leu Gly Ser Phe	
435	440	445
Lys Glu Thr Phe Tyr Lys His	Ser Pro Glu Ala Phe Ser Leu Ser Lys	
450	455	460
Ala Glu Lys Pro Asp Cys Met	Glu Arg Leu Gln Leu Gln Arg Arg Leu	
465	470	475
Gly Cys Arg Thr Phe His Trp	Phe Leu Ala Asn Val Tyr Pro Glu Leu	
485	490	495
Tyr Pro Ser Glu Pro Arg Pro	Ser Phe Ser Gly Lys Leu His Asn Thr	
500	505	510
Gly Leu Gly Leu Cys Ala Asp	Cys Gln Ala Glu Gly Asp Ile Leu Gly	
515	520	525
Cys Pro Met Val Leu Ala Pro	Cys Ser Asp Ser Arg Gln Gln Gln Tyr	
530	535	540
Leu Gln His Thr Ser Arg Lys	Glu Ile His Phe Gly Ser Pro Gln His	
545	550	555
Leu Cys Phe Ala Val Arg Gln	Glu Gln Val Ile Leu Gln Asn Cys Thr	
565	570	575
Glu Glu Gly Leu Ala Ile His	Gln Gln His Trp Asp Phe Gln Glu Asn	
580	585	590
Gly Met Ile Val His Ile Leu	Ser Gly Lys Cys Met Glu Ala Val Val	
595	600	605
Gln Glu Asn Asn Lys Asp Leu	Tyr Leu Arg Pro Cys Asp Gly Lys Ala	
610	615	620
Arg Gln Gln Trp Arg Phe Asp	Gln Ile Asn Ala Val Asp Glu Arg	
625	630	635

<210> 347  
 <211> 1891  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1891)  
 <223> n = A,T,C or G

<400> 347

358

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cacagtcaact actgtcgcct cagctgggaa cattggggag gatggaatcc tgagctgcac 240
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caagggaat gctaaccttg agtataaaac tggagccttc agcatgccgg aagtgaatgt 540
ggactataat gccagctcag agaccttgcg gtgtgaggct ccccgatggt tccccagcc 600
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nttcaagna gaatgnattw aaaatatacy attttccbaa aaaaaaaaaa aaaaaaaaaa 1860
maaagtacct cggccgcgac cagcctaagg g 1891

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&lt;210&gt; 348

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 348

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Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
  1             5             10             15
Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
      20             25             30
Gly Arg His Ser Ile Thr Val Thr Val Ala Ser Ala Gly Asn Ile
      35             40             45
Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
      50             55             60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
      65             70             75             80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
      85             90             95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
      100            105            110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
      115            120            125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
      130            135            140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn

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359

145		150		155		160
Ala Ser Ser Glu Thr	Leu Arg Cys Glu Ala	Pro Arg Trp Phe Pro Gln				
	165	170		175		
Pro Thr Val Val Trp	Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser					
	180	185		190		
Glu Val Ser Asn Thr	Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met					
	195	200		205		
Lys Val Val Ser Val	Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser					
	210	215		220		
Cys Met Ile Glu Asn	Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val					
	225	230		235		240
Thr Glu Ser Glu Ile	Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser					
	245	250		255		
Lys Ala Ser Leu Cys	Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu					
	260	265		270		
Leu Pro Leu Ser Pro	Tyr Leu Met Leu Lys					
	275	280				

&lt;210&gt; 349

&lt;211&gt; 1517

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1517)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 349

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&lt;210&gt; 350

360

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 <213> Homo sapiens  
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 <221> VARIANT  
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 35 40 45  
 Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp  
 50 55 60  
 Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met  
 65 70 75 80  
 Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp  
 85 90 95  
 Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr  
 100 105 110  
 Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe  
 115 120 125  
 Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg  
 130 135 140  
 Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser  
 145 150 155 160  
 Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln  
 165 170 175  
 Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala  
 180 185 190  
 Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser  
 195 200 205  
 Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Xaa Xaa Gln Arg  
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 Leu Asp Gly

<210> 351  
 <211> 248  
 <212> PRT  
 <213> Homo sapiens

<400> 351  
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 35 40 45  
 Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp  
 50 55 60

361

Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met  
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 Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp  
 85 90 95  
 Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr  
 100 105 110  
 Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe  
 115 120 125  
 Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg  
 130 135 140  
 Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser  
 145 150 155 160  
 Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln  
 165 170 175  
 Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala  
 180 185 190  
 Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser  
 195 200 205  
 Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Lys Gly Ser Ala  
 210 215 220  
 Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys Ser Ser Phe Ile  
 225 230 235 240  
 Leu Met Asp Asp Leu Ser Pro Lys  
 245

&lt;210&gt; 352

&lt;211&gt; 1529

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1529)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 352

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362

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&lt;210&gt; 353

&lt;211&gt; 252

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 353

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			20					25					30		
Ser	Asp	Leu	Ser	Gln	Val	Phe	Gln	Pro	Tyr	Thr	Leu	Arg	Thr	Arg	Arg
		35					40					45			
Asn	Ser	Thr	Thr	Ile	Met	Ser	Arg	His	Ser	Leu	Val	Ser	Ile	Glu	Glu
		50				55					60				
Glu	Gly	Leu	Asp	Met	Val	Asn	Arg	Glu	Thr	Ala	His	Glu	Arg	Glu	Met
65					70					75					80
Gln	Thr	Ala	Met	Gln	Ile	Ser	Gln	Ser	Trp	Asp	Glu	Ser	Leu	Ser	Leu
				85					90					95	
Ser	Asp	Ser	Asp	Phe	Asp	Lys	Pro	Glu	Lys	Leu	Tyr	Ser	Pro	Lys	Arg
			100					105					110		
Ile	Asp	Phe	Thr	Pro	Val	Ser	Pro	Ala	Pro	Ser	Pro	Thr	Arg	Gly	Phe
		115					120						125		
Gly	Lys	Met	Phe	Val	Ser	Ser	Ser	Gly	Leu	Pro	Pro	Ser	Pro	Val	Pro
		130				135					140				
Ser	Pro	Arg	Arg	Phe	Ser	Ser	Arg	Arg	Ser	Gln	Ser	Pro	Val	Lys	Cys
145					150					155					160
Ile	Arg	Pro	Ser	Val	Leu	Gly	Pro	Leu	Lys	Arg	Lys	Gly	Glu	Met	Glu
				165					170					175	
Thr	Glu	Ser	Gln	Pro	Lys	Arg	Leu	Phe	Gln	Gly	Thr	Thr	Asn	Met	Leu
			180					185					190		
Ser	Pro	Asp	Ala	Ala	Gln	Leu	Ser	Asp	Leu	Ser	Ser	Cys	Ser	Asp	Ile
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Leu	Asp	Gly	Ser	Ser	Ser	Ser	Ser	Gly	Leu	Ser	Ser	Asp	Pro	Leu	Ala
		210				215					220				
Lys	Gly	Ser	Ala	Thr	Ala	Glu	Ser	Pro	Val	Ala	Cys	Ser	Asn	Ser	Cys
225					230					235					240
Ser	Ser	Phe	Ile	Leu	Met	Asp	Asp	Leu	Ser	Pro	Lys				
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&lt;210&gt; 354

&lt;211&gt; 1574

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1574)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 354

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&lt;210&gt; 355

&lt;211&gt; 267

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 355

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Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu
20      25      30
Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg
35      40      45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Leu Leu Ser Ser Ser
50      55      60
Pro Asn Arg Ile Pro Ser Ser Arg Leu His Gln Ile Lys Arg Glu Glu
65      70      75      80
Gly Leu Asp Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln
85      90      95
Thr Ala Met Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser
100     105     110
Asp Ser Asp Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile
115     120     125
Asp Phe Thr Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly
130     135     140
Lys Met Phe Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser
145     150     155     160
Pro Arg Arg Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile
165     170     175
Arg Pro Ser Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr
180     185     190
Glu Ser Gln Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser

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364

195	200	205
Pro Asp Ala Ala Gln Leu Ser	Asp Leu Ser Ser	Cys Ser Asp Ile Leu
210	215	220
Asp Gly Ser Ser Ser Ser	Gly Leu Ser Ser	Asp Pro Leu Ala Lys
225	230	235
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245	250	255
Ser Phe Ile Leu Met Asp Asp	Leu Ser Pro Lys	
260	265	

<210> 356  
 <211> 4458  
 <212> DNA  
 <213> Homo sapiens

<400> 356

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aaaaaaaaa aaaaaaa 4458

```

&lt;210&gt; 357

&lt;211&gt; 127

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 357

```

Met Pro Arg Trp Leu Leu Ser Leu Thr Phe Ala Gly Leu Phe Pro
1          5          10          15
Leu Arg Arg Arg Gln Leu Leu Gly Ser Cys Gly Gly Arg Glu Gly Gly
20          25          30
Gly Pro Asp Gln Pro Ala Gly Ser Pro Ala Pro Leu Arg Pro Pro Leu
35          40          45
Pro Arg Thr Leu Arg Leu Arg Lys Tyr Arg Gly Asn Pro Leu Pro Pro
50          55          60
Glu Val Arg Gly Ser Leu Pro Glu Gly Ala Pro Trp Ser Arg Ala Pro
65          70          75          80
Leu Gly Gly His Leu Glu Ala Arg Cys Gly Pro Arg Thr Arg Glu Glu
85          90          95
Arg Ala Ala Gly Ala Ala Ala Thr Ala Gly Gly Gly Ala Gly Ser Pro
100          105          110
Gly Ala Ala Glu Gly Arg Pro Val Leu His Met Leu Pro Leu Gly
115          120          125

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<210> 358  
 <211> 1168  
 <212> DNA  
 <213> Homo sapiens

<400> 358  
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 cagaccaacc ggctggcagc ccagctccgc tccgcccgcg cctgcctcgg accctgcgcc 180  
 tgaggaagta tccaggcaac cctctgccac ccgaagtctg tgggtcgctc ccagaggcg 240  
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<210> 359  
 <211> 4458  
 <212> DNA  
 <213> Homo sapiens

<400> 359  
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 cagaccaacc ggctggcagc ccagctccgc tccgcccgcg cctgcctcgg accctgcgcc 180  
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aaaaaaaaa aaaaaaaa

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&lt;210&gt; 360

&lt;211&gt; 583

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 360

368

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aagactggcg tgtgccccga gctccagggt gaccagaact gcacgcaaga gtgctgtctcg 180
gacagcgaat gcgcgcgaca cctcaagtgc tgcagcgcg gctgtgccac cttctgcctt 240
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<210> 361  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

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<400> 361
Met Pro Ala Cys Arg Leu Gly Pro Leu Ala Ala Ala Leu Leu Leu Ser
1          5          10          15
Leu Leu Leu Phe Gly Phe Thr Leu Val Ser Gly Thr Gly Ala Glu Lys
20          25          30
Thr Gly Val Cys Pro Glu Leu Gln Ala Asp Gln Asn Cys Thr Gln Glu
35          40          45
Cys Val Ser Asp Ser Glu Cys Ala Asp Asn Leu Lys Cys Cys Ser Ala
50          55          60
Gly Cys Ala Thr Phe Cys Leu Leu Cys Pro Asn Asp Lys Glu Gly Ser
65          70          75          80
Cys Pro Gln Val Asn Ile Asn Phe Pro Gln Leu Gly Leu Cys Arg Asp
85          90          95
Gln Cys Gln Val Asp Thr Gln Cys Pro Gly Gln Met Lys Cys Cys Arg
100         105         110
Asn Gly Cys Gly Lys Val Ser Cys Val Thr Pro Asn Phe
115         120         125

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<210> 362  
 <211> 3310  
 <212> DNA  
 <213> Homo sapiens

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<400> 362
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369

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&lt;210&gt; 363

&lt;211&gt; 732

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 363

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Met Val Arg Ser Gly Asn Lys Ala Ala Val Val Leu Cys Met Asp Val
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Gly Phe Thr Met Ser Asn Ser Ile Pro Gly Ile Glu Ser Pro Phe Glu
20      25      30
Gln Ala Lys Lys Val Ile Thr Met Phe Val Gln Arg Gln Val Phe Ala
35      40      45
Glu Asn Lys Asp Glu Ile Ala Leu Val Leu Phe Gly Thr Asp Gly Thr
50      55      60
Asp Asn Pro Leu Ser Gly Gly Asp Gln Tyr Gln Asn Ile Thr Val His
65      70      75      80
Arg His Leu Met Leu Pro Asp Phe Asp Leu Leu Glu Asp Ile Glu Ser
85      90      95

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370

Lys Ile Gln Pro Gly Ser Gln Gln Ala Asp Phe Leu Asp Ala Leu Ile  
 100 105 110  
 Val Ser Met Asp Val Ile Gln His Glu Thr Ile Gly Lys Lys Phe Glu  
 115 120 125  
 Lys Arg His Ile Glu Ile Phe Thr Asp Leu Ser Ser Arg Phe Ser Lys  
 130 135 140  
 Ser Gln Leu Asp Ile Ile Ile His Ser Leu Lys Lys Cys Asp Ile Ser  
 145 150 155 160  
 Leu Gln Phe Phe Leu Pro Phe Ser Leu Gly Lys Glu Asp Gly Ser Gly  
 165 170 175  
 Asp Arg Gly Asp Gly Pro Phe Arg Leu Gly Gly His Gly Pro Ser Phe  
 180 185 190  
 Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu Gly Leu Glu Ile Val  
 195 200 205  
 Lys Met Val Met Ile Ser Leu Glu Gly Glu Asp Gly Leu Asp Glu Ile  
 210 215 220  
 Tyr Ser Phe Ser Glu Ser Leu Arg Lys Leu Cys Val Phe Lys Lys Ile  
 225 230 235 240  
 Glu Arg His Ser Ile His Trp Pro Cys Arg Leu Thr Ile Gly Ser Asn  
 245 250 255  
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 260 265 270  
 Lys Lys Thr Trp Thr Val Val Asp Ala Lys Thr Leu Lys Lys Glu Asp  
 275 280 285  
 Ile Gln Lys Glu Thr Val Tyr Cys Leu Asn Asp Asp Asp Glu Thr Glu  
 290 295 300  
 Val Leu Lys Glu Asp Ile Ile Gln Gly Phe Arg Tyr Gly Ser Asp Ile  
 305 310 315 320  
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 325 330 335  
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 370 375 380  
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 385 390 395 400  
 Ala Asn Pro Gln Val Gly Val Ala Phe Pro His Ile Lys His Asn Tyr  
 405 410 415  
 Glu Cys Leu Val Tyr Val Gln Leu Pro Phe Met Glu Asp Leu Arg Gln  
 420 425 430  
 Tyr Met Phe Ser Ser Leu Lys Asn Ser Lys Lys Tyr Ala Pro Thr Glu  
 435 440 445  
 Ala Gln Leu Asn Ala Val Asp Ala Leu Ile Asp Ser Met Ser Leu Ala  
 450 455 460  
 Lys Lys Asp Glu Lys Thr Asp Thr Leu Glu Asp Leu Phe Pro Thr Thr  
 465 470 475 480  
 Lys Ile Pro Asn Pro Arg Phe Gln Arg Leu Phe Gln Cys Leu Leu His  
 485 490 495  
 Arg Ala Leu His Pro Arg Glu Pro Leu Pro Pro Ile Gln Gln His Ile  
 500 505 510  
 Trp Asn Met Leu Asn Pro Pro Ala Glu Val Thr Thr Lys Ser Gln Ile  
 515 520 525  
 Pro Leu Ser Lys Ile Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys  
 530 535 540  
 Lys Asp Gln Val Thr Ala Gln Glu Ile Phe Gln Asp Asn His Glu Asp  
 545 550 555 560

371

Gly	Pro	Thr	Ala	Lys	Lys	Leu	Lys	Thr	Glu	Gln	Gly	Gly	Ala	His	Phe
				565					570					575	
Ser	Val	Ser	Ser	Leu	Ala	Glu	Gly	Ser	Val	Thr	Ser	Val	Gly	Ser	Val
			580					585					590		
Asn	Pro	Ala	Glu	Asn	Phe	Arg	Val	Leu	Val	Lys	Gln	Lys	Lys	Ala	Ser
		595					600					605			
Phe	Glu	Glu	Ala	Ser	Asn	Gln	Leu	Ile	Asn	His	Ile	Glu	Gln	Phe	Leu
	610					615					620				
Asp	Thr	Asn	Glu	Thr	Pro	Tyr	Phe	Met	Lys	Ser	Ile	Asp	Cys	Ile	Arg
625					630					635				640	
Ala	Phe	Arg	Glu	Glu	Ala	Ile	Lys	Phe	Ser	Glu	Glu	Gln	Arg	Phe	Asn
			645						650					655	
Asn	Phe	Leu	Lys	Ala	Leu	Gln	Glu	Lys	Val	Glu	Ile	Lys	Gln	Leu	Asn
			660					665					670		
His	Phe	Trp	Glu	Ile	Val	Val	Gln	Asp	Gly	Ile	Thr	Leu	Ile	Thr	Lys
		675					680					685			
Glu	Glu	Ala	Ser	Gly	Ser	Ser	Val	Thr	Ala	Glu	Glu	Ala	Lys	Lys	Phe
	690					695					700				
Leu	Ala	Pro	Lys	Asp	Lys	Pro	Ser	Gly	Asp	Thr	Ala	Ala	Val	Phe	Glu
705					710					715					720
Glu	Gly	Gly	Asp	Val	Asp	Asp	Leu	Leu	Asp	Met	Ile				
				725					730						

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ning of each regular issue of the PCT Gazette.

(54) Title: NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION, ASSESSMENT, PREVENTION,  
AND THERAPY OF OVARIAN CANCER

(57) Abstract: The invention relates to newly discovered nucleic acid molecules and proteins associated with ovarian cancer. Com-  
positions, kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.



WO 02/071928 A3



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/07826

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :C07H 21/04, 21/02

US CL :536/23.1, 24.31, 24.33

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 24.31, 24.33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, DIALOG ONESEARCH ovary, ovarian, tumor, cancer, expression, level, marker, RNA, DNA, polynucleotide, oligonucleotide,

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,976,799 A (O'BRIEN et al) 02 November 1999, column 2, lines 27-47.	1
Y	US 5,709,999 A (SHATTUCK-EIDENS et al.) 20 January 1998, column 8, lines 38-67; column 15, lines 52-56; column 69, lines 26-30.	1
Y	US 6,087,125 A (BANDMAN et al) 11 July 2000, column 3, lines 15-25.	1
Y	WO 96/05308 A1 (MYRIAD GENTICS, INC) 22 February 1996, page 3, lines 9-17; page 12, lines 2-11; page 21, lines 24-25	1

☐ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Z" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/07826

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1, SEQ ID NO:1

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Groups 1-198, claim(s)1-198, each drawn to a different method of detecting ovarian cancer.

The inventions listed as Groups 1-198 do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claim 1 comprises 198 different methods each defined by a different nucleotide sequence each of which constitutes a different special technical feature and therefore a different invention. Thus, there is no single special technical feature in claim 1 nor a single inventive group. PCT Rule 13 permits a product, process of making the product and process of using the product in an inventive group but does not permit multiple methods of the same type in an inventive group